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BEHAVIOR DISORDERS OF INTELLECTUAL ORIGIN OCCURRING IN CHILDHOOD

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In the considerations given to the behavior disorders occurring in children, great attention has been paid, and justly, to emotional causes. This type of disorder is commonly spoken of as "emotional frustration" or as "id frustration." In this communication we wish to call attention to those behavior disorders in children in which the primary cause is a lack of adequate outlets for intellectual needs. From the artificial separation of the emotional and the intellectual facets of mental activity a certain amount of distortion necessarily results. The justification for this arbitrary division rests solely on the means it affords for isolating the functional characteristics of each aspect.

The problem of behavior and its disorders is properly the concern of psychiatric thought and research. No psychiatric material is so well adapted to the delineation and study of these disorders as the so-called problem child. This adaptability is the result of a number of factors. The child is biologic material which is very pliable. He has not yet accumulated a sufficiently tangled web of experience to make the untangling as difficult as in the adult who manifests a behavior disorder. Then, too, it is more frequently possible to make environmental adjustments in the case of the child. A third, and most important, factor is the naiveté of the child, which, because of his lack of experience or native aversion to hypocrisy and subterfuge, makes the eliciting of dependable psychiatric data easier.

The question of causation of behavior disorders in children is naturally important. Broadly speaking, the cause is always some lack

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of harmony between the child and his environment. Recognition of this fact is necessary to avoid the scientific solecism of regarding the child as an object to be studied in an environment-less vacuum, a consideration unlikely to lead to valid deductions or conclusions. In the present study the child is considered as the product of his own reaction to his environment. This consideration does away with the necessity for using such terms as "good child," "bad child," "good environment" and "bad environment." Psychiatrists are familiar with the pitfalls of using the moral adjectives "good" and "bad."

Disharmony between the person and his environment may come about in several ways. One of the most important is frustration of some particular personal need. Much has been said and written about emotional frustrations, the manifestations of which are often complicated. But other types of frustration exist, some of which are rather less complicated, perhaps even superficial—to mention a few trivial examples: the driving of a car through busy city traffic, with growing irritability on the part of the driver; a prolonged and unusual delay in the dinner hour, or consistent losing in a bridge game. Other less trivial frustrations may occur—prolonged periods of financial stress, loss of loved friends or relatives or chronic physical illness.

The type of frustration with which this paper is concerned might be called "intellectual frustration." By this term is meant a disharmony between the intellectual capacity of a person and the provision of proper outlets for that capacity by the environment. The disharmony is signalized by behavior disorders which show certain points of specificity but are not wholly pathognomonic. Of those frustrations essentially resulting from a lack of outlets for emotional drives, this communication will have little to say.

Because the behavior of the person is his reaction to the environment, it would be expected that any significant amount of disharmony in any direction would affect many diverse aspects of that behavior. For example, an anxiety state, which presumably represents a sort of emotional frustration, nearly always results in a lowering of intellectual output or efficiency. In intellectual frustration, many of the resulting symptoms are deeply concerned with emotional difficulties.

Since children are less free to adjust their own environments than adults, intellectual disharmony is more common in early life. As the child grows older he has more freedom to adjust his environment and behavior disorders due to lack of intellectual outlets become less common. While intellectual frustrations tend to be more common in intellectually superior children, whose demands on the environment are greater, they are not confined to such children, or even to children alone. Adults have shown essentially similar behavior disorders, with similar causation.

The 7 cases here presented all concerned children from 4 to 16 years old. Each presented a marked behavior problem and was brought

for psychiatric treatment. Psychometric measurements of each child revealed a mental age greater than the chronologic age. The therapeutic result in each instance appeared satisfactory.

REPORT OF CASES

CASE 1.—The patient, a 10 year old girl, had a mental age of 14. She was brought for psychiatric attention because she was having difficulties with her parents. She also was said to be a "fussy eater." Her school work had lately become poor. She had done well in school until she was 8, after which her work showed a distinct falling off, although she had never failed of promotion. The school's complaint was that she paid little attention to her work. Her parents said she was difficult to manage, particularly when at the table. She frequently tried to contribute to the conversation at the table, but her parents frowned on this and rebuked her with "Children should be seen, not heard."

During six interviews the child seemed alert and intelligent. She was somewhat resentful at first at being brought to a physician but soon grasped the opportunities the freedom of the interview hours gave her. She had read more widely than wisely. Her chief complaint about school classes was that they were "so slow." This large tempo in the classroom at first irritated her; later she learned to think of other matters during class hours. At home she was "never let to do anything" because she was "too young." The constant suppression, both at home and at school, had resulted in her becoming an aggressive, antagonistic and wilful child who had no sense of security, but only a feeling of frustration.

Her mother was seen twice and the situation was pointed out to her. The child subsequently was given more opportunity for expansion at home when her mental capabilities were more fully realized. She was also placed in a private school with small classes. Under this regimen her behavior difficulties ceased rather abruptly. From a follow-up telephone conversation eighteen months later it was learned that she had had no further difficulties.

CASE 2.—The patient was a boy of 10 years with a mental age of 16. He had been expelled repeatedly from school for "sex delinquencies." He had lost his father one year before and was possessed of an extraordinarily stupid and vicious mother, who remarked that she "didn't suppose anything could be done except to send him to reform school." The school reported that his expulsions were the result of his apprehension in homosexual practices with other students.

The boy had four interviews. At first he was somewhat sullen. He appeared bewildered and harassed, but his conversation soon demonstrated his marked intellectual superiority. He talked eagerly, as if a plug had been removed from his conversational reservoir. He had become restless and bored at school, both in class and at play. The children his own age were "too dumb" and those whom he regarded as equals would have none of him because he was too little. These older boys had apparently sensed that his eagerness for acceptance by their group would make him a ready proselyte for their sexual activities. Their judgment proved correct, but the pleasure he took in his acceptance, however dearly bought, turned to baffled panic when the consequences of discovery descended on him. In these overt sexual activities he was the passive member. As he talked and had some of his questions answered, he became at first more calm, then mildly aggressive toward the boys who had "tricked" him.

At this time it was regarded as inadvisable to attempt any fundamental investigation into the emotional aspects of the situation. It was discovered that he had a flair for drawing, and arrangements were made for private art lessons, which

furnished a satisfactory outlet for his intellectual needs. These, coupled with his admission to a high school, were regarded as a sufficient adjustment. In a telephone conversation ten months later it was reported that he had no particular difficulties and was doing exceptionally well with his art and at school.

CASE 3.—The patient was a boy of 6 years with a mental age of 9. He was brought by an extremely solicitous mother. He was an only child, born to his mother when she was 39. Her sterility up to that time had been a source of great emotional conflict. She complained that her son had a "vicious temper." It was evident that the mother wished to keep the boy an infant: he had long hair and wore "sissy" suits. Nocturnal enuresis had been present since birth. It was reported that he was extremely disobedient and a "foot stamper." His mother had a protective, overdirective attitude toward him and was hurt and puzzled by his aggressive behavior toward her. He had not yet been sent to school and was given simple building blocks and the like for toys.

The boy was seen for ten interviews. One of the first things he said was: "Doctor, I'm glad you aren't going to use baby talk with me." He showed every evidence of being more mature intellectually than his chronologic age would indicate. After the first of the interviews he expressed great satisfaction that they were to continue for a time. Most of the time was spent in talking and little on the toys provided. He had a keen sense of logic, particularly in regard to his mother's treatment of him. During the course of the interviews his enuresis all but completely stopped.

Work with the mother was instituted only with respect to enabling her to orient the boy and herself in this particular situation. It was pointed out that her long period of childlessness and the fact that the number of her offspring was limited to one had resulted in the present unjustifiable situation. It was also stressed that she had been attempting to treat as 3 years old a child with a 9 year old intellect. The boy was given more suitable playthings and started to go to school. From a follow-up investigation after eight months it was learned that he was in the third year at school and apparently well adjusted.

CASE 4.—The patient was a girl of 4 years with a mental age of 7. She was brought because of her aggressive behavior, which included temper tantrums, fighting with her brother and sister and a disobedient attitude toward her parents. She had always been an active child, but in the last year she had "overrun all bounds." She refused to take her naps in the afternoons and, disdaining her own toys, would play only with those of her older brother and sister. They objected to the appropriation of their toys, and arguments were frequent. In spite of the mother's annoyance at these behavior difficulties, she thought the child "cute" and that she said "the cleverest things." The patient had always been in good physical health and was somewhat oversized for her age.

In ten interviews the child was well behaved and talkative. She complained that everybody tried to "make a baby" of her and that she was "sick of it." She had a well rounded speaking vocabulary and a written vocabulary of about twenty words, which she had picked up from her older siblings. She had no deep-seated animosity toward her parents but resented their stopping her from "doing anything." She liked to play with her brother and sister but had no friends of her own age.

Her mother was seen four times, and some attempt was made to explain that this child had an intellectual maturity close to those of her older children and that for this reason she would need the same intellectual opportunities at home and in a school. Subsequently she was placed in a small private school, where she progressed rapidly. Her behavior disorders ceased abruptly with these opportunities for intellectual activity.

CASE 5.—The patient was a boy of 9 years with a mental age of 10. He was brought with the statement that "he has nasty habits," which apparently consisted of sexual play with his sister, aged 8. He was a large, healthy boy with a few pubic hairs and beginning pigmentation of his genitalia, which were moderately large. No physical abnormalities were found. Other complaints concerning his behavior included specifications of aggressive conduct toward his parents, teachers and playmates. His mother's attitude had been one of overprotection and is best exemplified by the fact that he had bobbed hair until the age of 8.

He was seen twelve times in all. He was rather polite but somewhat impetuous. His school work had been relatively poor, but he had always obtained promotion. He did not like school work, because there "was nothing to it." As a consequence, he was inattentive. His comprehension was quick and his originality of thought striking. Apparently the sexual play which resulted in his being brought for treatment was largely motivated by curiosity rather than by any definite objective. He was dismayed by the consequences of his behavior. It was explained to him that a good way to behave is to do things one wants to with respect to "the policeman around the corner." He readily grasped this concept. During the course of the interviews it was reported that his behavior had improved considerably.

His mother was urged to be more passive about him and to give him more outlets for his quick intelligence. He joined the Boy Scout Cubs and became interested in photography, which seemed to provide adequate outlets for his previously suppressed intellectual energies.

CASE 6.—The patient was a girl of 16 years with a mental age of 18. She was brought by her mother and was tearful and irritable. Her mother complained that the girl was "very stubborn" and would not "listen to anybody." The patient was an only child. She wore clothes suited to a girl of 13 or 14, although she was mature and pretty. Her mother, who was relatively unintelligent, mentioned suspiciously that the father was much closer to the daughter than she was and accompanied this statement with typical futile gestures of her hands. She then hesitantly mentioned: "She is beginning to notice boys, I'm afraid."

The patient herself was in a distracted state. Any logical attempts she may have made to solve her own problems had been thwarted by her mother's constant carpings. When treated as an adult she calmed down considerably, and it was interesting to see the avidity with which she talked on intellectual subjects. She was a prodigious reader and eagerly adopted many of the suggestions made about books to read.

After several interviews she spoke of a plan she had been formulating to go to college. She thought she would be able to pass certifying examinations in high school subjects and use this certification as a means of entering college. This would eliminate the necessity of continuing at a low-geared high school. She carried this plan through, to the astonishment of her mother, and was able to enter college the following fall. Reports have been received from time to time. She is leading an active scholastic and athletic life, which satisfies her but vaguely annoys her perplexed mother.

CASE 7.—The patient was a boy of 9 years with a mental age of 10, who had been having trouble with his teachers. He had done well in school, both in studies and in athletics, until the present term. Notes reached his parents, occasionally at first, then more frequently. These notes centered mainly about his misconduct in a science class.

He was an omnivorous reader, often of works more abstruse than his mental age would warrant. Perusal of these books often left him with a great many

questions for which his natural curiosity sought answers. He attempted to get these answers from his uninterested and none too well prepared teacher. When she attempted to bluff, the cold, steely logic of the boy frequently reduced her answers to absurdity. In our interviews it soon became apparent that he had begun to realize that he had a great many mental attributes his teacher did not possess. She had tried sarcasm and similar means to reduce him to silence, but with the eyes of the class on him he could not remain silent. This teacher-pupil rivalry became worse when he noticed that when his teacher made a statement the class would turn to him for either his silent confirmation or his vociferous disapproval. Soon this sense of superiority and his desire for recognition resulted in his adopting a rather belligerent attitude toward other teachers as well, and the vicious circle was in full swing.

He was the only son of middle class, fairly intelligent parents. He was neat and moderately careful about his clothes. He had never been in any special difficulties before.

At first he was antagonistic toward the interviewer, but nothing was done to dispel his antagonism except to conceal its recognition. Before each visit he would look up especially difficult points with which to try to trap his interviewer. He was seen nine times in all, at weekly interviews, to which he was accompanied by his mother the first seven times and then twice came alone. It gradually became possible to indicate that he had no need to establish himself by stepping on others and that it would be pleasant to establish himself on his own merits. He was shown, without going into his belligerency, that he could answer many of his own questions if he took the time and that no one person could ever say the last word on any subject. He took to the business of finding his own answers very well and was noticeably less belligerent and more agreeable. A follow-up telephone conversation six months later revealed he was still doing well.

These patients seem to be representative of those with behavior disorders founded on intellectual suppression. With 1 questionable exception (case 5) the children were all intellectually definitely superior. Each showed evidence of an essential disharmony between his intellectual capacity and the outlets for that capacity provided by his environment. The prompt therapeutic response to the provision of more adequate intellectual outlets indicates that the disharmony was probably causal. There is no other etiologic group of childhood behavior disorders in which any type of therapeusis is so dramatically effective.

There are, in addition to high psychometric readings, other clinical features which are of interest. No evidence of marked anxiety was seen in any of these children. There was no evidence of significant schizoid traits and no tendency toward unusual autistic thinking or daydreaming. Fantasy formation was slight, and the patients' discussions of their difficulties were largely factual. Drawings and play activities were intricate and explicit in design. Most of them were produced with care as to detail. An unusual degree of aggressiveness was present in all of the patients.

If one were to translate what has been said into psychoanalytic terms, the situation here described might be regarded as an "ego frustration." The fact that these children recovered so rapidly with appropriate treat-

ment would indicate that no deep-seated changes had occurred. However, the disorders of all these children were considered recent in that the patients were seen before their symptoms became intricate and involved. One suspects that the persistence of the intellectual suppression over a prolonged period might have resulted in more serious, possibly irreparable, damage.

The emotional factors in these patients were regarded as secondary to the suppression of intellectual interests. It might be argued that this viewpoint is superficial and that completed life histories of these patients would reveal deeply rooted personality disorders. Arguments based on future possibilities are not always productive of immediate gains, either in increasing the store of knowledge or in effecting therapeutic results. In the situations here presented, the sequence of events was so impressive that the simple explanation advanced seems justified. As stated before, it is only to be expected that disturbances in one sphere of mental activity would produce changes in mental equilibriums which might affect all spheres. The type and extent of these secondary emotional symptoms are determined by the structure of the individual personality. At any rate, these children dealt adequately with their own problems when the proper intellectual outlets were provided.

Overcrowded, understaffed schools favor the development of this type of behavior disorder. In those schools or school systems which take cognizance of the presence of superior children special educational environments are provided. One of these is the "speed up" system, in which the child does his work in less time than other children. Another is the enrichment program, in which he is given more collateral work than other children. The latter is ordinarily the wiser choice, as the child is enabled to answer most of the questions prompted by his intellectual curiosity. In either system superior teachers are necessary.

The problem is not one of schooling alone. The child whose intellectual superiority is poorly understood at home may experience enough intellectual suppression for behavior difficulties to develop. An understanding, not overly ambitious handling at home will do much to save these children from behavior difficulties.

It is our impression that difficulties are much more prone to develop in superior children and adults than in those not similarly endowed. However, the expenditure of considerable effort would seem justified to preserve health of mind and personality in such persons for the efficient performance of those useful functions of which they alone are capable.

POSSIBLE RELATION BETWEEN ELECTROLYTE BALANCE AND BRONCHIAL ASTHMA

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Several years ago one of us (A. V. S.) observed the advantageous effect of the ingestion of large amounts of dextrose in children with bronchial asthma.[1] About the same time McQuarrie, Thompson and Anderson[2] called attention to the favorable influence of diets high in salt on the carbohydrate metabolism of diabetic children. The question then arose as to whether the ingestion of large amounts of sodium chloride would affect the benefits derived from the high carbohydrate diet in asthmatic children. The first few trials with a diet high in salt produced in each instance a definite increase in the asthmatic symptoms. Lowering the salt decreased the asthmatic symptoms, and this effect was enhanced by either short periods of artificial fever or the ingestion of potassium chloride.[3] These observations led to an investigation of the electrolyte metabolism in children with bronchial asthma.

MATERIALS AND METHODS

Twelve children and young adults in whom asthma persisted in spite of the best allergic management were observed under the standard metabolic conditions customary in pediatric wards. The patients ranged from 4 to 18 years in age. Repeated studies were carried out on each patient. Only 1 child was under observation at one time. At such a time he was kept in a small metabolism room under the constant supervision of nurses carefully instructed in his care, who weighed the child, collected and stored the urine and feces in special containers and made certain that diets and medications were taken precisely as ordered.

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1. Stoesser, A. V.: Recent Observations in the Study of Asthma Due to Food Allergy, J. Allergy **3**:332, 1932.

2. McQuarrie, I.; Thompson, W. H., and Anderson, J. A.: Effects of Excessive Ingestion of Sodium and Potassium Salts on Carbohydrate Metabolism and Blood Pressure in Diabetic Children, J. Nutrition **11**:77, 1936.

3. Cook, M. M., and Stoesser, A. V.: Influence of Induced Variations in Electrolyte and Water Exchanges with Pitressin in Bronchial Asthma, Proc. Soc. Exper. Biol. & Med. **38**:636, 1938.

The room temperature was held between 68 and 74 F. and the relative humidity between 40 and 60 per cent to prevent perspiring or chilling. The body weight was determined on a metabolism balance every twenty-four hours. This was done immediately after the bladder was emptied and before food or water was given. With the same mercury sphygmomanometer, measurements of systolic and diastolic blood pressure were made on some of the children before meals and after they had been at rest for at least half an hour. The severity of asthma was determined by hourly observations day and night by one of us (M. M. C.), and the number of doses of epinephrine required to give the patient some comfort was recorded. The degree of severity of the asthma was represented by the following code of arbitrary units:

0—No asthmatic wheezing observed and no epinephrine used.

1—Wheezing present at least one hour per day, requiring one dose of epinephrine.

2—Wheezing present three hours per day, requiring usually three doses of epinephrine.

TABLE 1.—*Foods and Proportions of Diet 1* *

Food	Amount †	Protein †	Fat †	Carbohydrate †
White bread	40	3.72	0.48	21.08
Powdered whole milk	13	3.46	3.64	4.94
Egg yolk	16	2.51	5.33	....
Egg white	44	5.41	0.09	....
Cream, 40%	36	0.79	14.40	1.08
Clear lemon juice	12	....	.....	1.18
Unsalted butter	13	0.13	11.05	....
Yeast	1	0.12	.....	....
Sugar, powdered and granulated	28	....	.....	28.00
		16.14	34.99	56.28

* Six hundred grams of distilled water was allowed. The water not used in cooking was measured out for drinking.

† All measurements are in grams.

3—Wheezing present about half the time, or at least twelve hours per day, requiring about five doses of epinephrine per day.

4—Continuous wheezing, requiring eight or more doses of epinephrine per day.

5 to 7—Continuous severe wheezing present, with little or no help from epinephrine.

Two special diets were employed during the experimental periods. The first one was similar to that of McQuarrie and his co-workers.[2] For the sake of uniformity and accuracy it was made up of the following foods in the proportions indicated in grams: white bread, 40; powdered whole milk, 13; egg yolk, 16; egg white, 44; 35 to 40 per cent cream, 36; clear lemon juice, 12; unsalted butter, 13; yeast, 1; cane sugar, 28, and distilled water, 600. This diet contained: protein, 16.14 Gm.; fat, 34.99 Gm., and carbohydrate, 56.28 Gm. (table 1). The mineral constituents, in grams, were as follows: sodium, 0.36; potassium, 0.32; calcium, 0.18; magnesium, 0.03; chloride, 0.62; phosphorus, 0.24, and sulfur, 0.20 (table 2). The amounts of protein, fat and carbohydrate were adjusted to meet the patients' caloric requirements. The same amount of food was given at each meal. The meals were equally spaced at six hour intervals, and between times the subjects were permitted to take measured amounts of distilled water.

The second diet was very simple. It consisted of egg yolk, 105 Gm.; 35 per cent cream, 105 Gm.; clear lemon juice, 63 Gm.; pure cane sugar, 193 Gm., and distilled water, 600 Gm. This formula contained protein, 18.87 Gm.; fat, 77.0 Gm., and carbohydrate, 201.99 Gm. The important mineral constituents were as follows: sodium, 0.12 Gm.; potassium, 0.33 Gm., and chloride, 0.18 Gm. The diet was relatively low in sodium, potassium and chloride. The children were given four evenly spaced daily feedings of this formula, which has reasonably adequate basal dietary constituents. The amount of the feeding, weighed out for each meal, depended on the initial weight of the patient. A small amount of vanilla was occasionally used to flavor the mixture. Vitamin requirements were met by adding thiamine hydrochloride (vitamin B_1), ascorbic acid (vitamin C) and a preparation of purified crystalline vitamin D in propylene glycol.[4] A few of the children received a preparation containing vitamins A, B_1, G (B_2), C and D.[5] Little difficulty was encountered in maintaining the subjects on the simple diet provided the experimental periods were not too long. When extra salts were added, they were given in the form of enteric-coated tablets.[6] The sodium chloride tablets contained 1 Gm. of the salt and the potassium chloride tablets 0.5 Gm.

TABLE 2.—*Mineral Constituents of Diet 1*

Food	Amount*	Na*	K*	Ca*	Mg*	Cl*	S*	P*	H_2O*
White bread.....	40	0.1606	0.0442	0.0107	0.0097	0.2479	0.0420	0.0377	14.120
Powdered whole milk.....	13	0.0549	0.1555	0.1086	0.0109	0.1086	0.0207	0.0796	0.195
Egg yolk.....	16	0.0120	0.0186	0.0216	0.0024	0.0150	0.0264	0.0835	7.920
Egg white.....	44	0.0201	0.0219	0.0051	0.0043	0.0693	0.0952	0.0061	37.972
Cream, 40%.....	36	0.0129	0.0453	0.0313	0.0043	0.0288	0.0115	0.0241	17.460
Clear lemon juice	12	0.0011	0.0152	0.0029	0.0012	0.0004	0.0007	0.0012	10.752
Unsalted butter..	13	0.1029	0.0021	0.0021	.....	0.1580	0.0010	0.0021	1.417
Yeast.....	1	0.0017	0.0242	0.0002	0.0012	0.0001	0.0045	0.0137	0.050
Sugar.....	28	.....	.....	.....	.....	.....	.....	.....	.....
		0.3662	0.3270	0.1825	0.0340	0.6251	0.2020	0.2480	89.886

* All measurements are in grams.

The chemical methods used for the analyses of the blood were as follows: potassium, Shohl and Bennett;[7] chloride, Wilson and Ball,[8] and sodium, Butler and Tuthill.[9]

Artificial fever therapy was given the subjects for three to five hour periods at temperatures ranging from 103 to 105 F. by means of a Simpson-Kettering hypertherm, which appeared similar to a Drinker respirator in that the patient's body was enclosed in the unit and his head protruded. Sliding side doors allowed access to the child's body for checking rectal temperatures and inspecting the skin. The temperature and humidity were under automatic control, but there were manual

4. The preparation used was drisdol.

5. The preparation used was vi-pentaperles "Roche."

6. Furnished by the Eli Lilly & Company Research Laboratories.

7. Shohl, A. T., and Bennett, H. B.: A Micro Method for the Determination of Potassium as Iodoplatinate, J. Biol. Chem. **78**:643, 1928.

8. Wilson, D. W., and Ball, E. G.: A Study of the Estimation of Chloride in Blood and Serum, J. Biol. Chem. **79**:221, 1928.

9. Butler, A. M., and Tuthill, E.: An Application of the Uranyl Zinc Acetate Method for Determination of Sodium in Biological Material, J. Biol. Chem. **93**: 171, 1931.

adjustments for regulation. Originally the fever therapy technic utilized cabinet temperatures as high as 140 to 160 F. Successive alterations in the mechanism and controls of the Kettering machine raised the relative humidity to 100 per cent and resulted in lowering operating temperatures to 110 or 115 F. This change increased the comfort of the patient, lowered the amount of sedatives required and reduced cutaneous complications, uncontrollable temperatures and vasomotor collapse to the vanishing point.[10] The safety features permitted repeated utilization of the machine in producing hyperpyrexia in the asthmatic patients.

RESULTS

For the sake of clearness the data from the most representative periods of the investigations on 4 of the 12 children have been condensed on graphic charts, which are largely self explanatory. They will now be briefly considered.

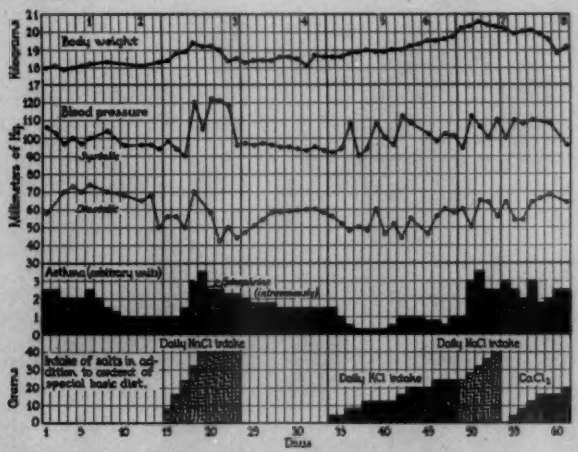

Chart 1.—Data obtained during a period of special study of M. M. D., an 8 year old girl with intractable asthma, revealing the beneficial influence of diet 1, low in sodium chloride, and the addition of potassium chloride, together with the deleterious effect of large amounts of sodium chloride and the lack of response to calcium chloride.

Chart 1 presents the data obtained during a two month period of observation on 1 of the first groups of children subjected to our studies. This child, an 8 year old girl, had had asthma more or less continuously for three years. The patient was admitted to the hospital and placed on diet 1. She was closely watched day and night by one of us (M. M. C.). For fifteen days the child remained quiet, and there was a gradual improvement in the asthma. The weight of the patient

10. Snow, W. B.: The Rationality, Practicability and Limitations of Induced Fever as a Therapeutic Agent, M. Rec. **148**:448, 1938.

remained constant, and no marked changes occurred in the blood pressure. On the sixteenth day, sodium chloride was administered in the hope that it might have a beneficial effect, thereby reducing the requirement for intramuscular injections of epinephrine. Beginning with 8 Gm. per day, the amount of salt given was increased to 40 Gm. in six days. The result was startling. The asthma became much worse, requiring on two consecutive days the intravenous administration of epinephrine. The patient's weight increased, owing to the greater intake and retention of water with the ingestion of salt. This was accompanied by a rise in the blood pressure, especially in the systolic pressure. After nine days of feeding sodium chloride, administration of the salt was discontinued abruptly and for the next ten days the patient received only diet 1. Again there was a gradual improvement, and the child was fairly comfortable. The weight dropped back to the original level, and the blood pressure returned to within the normal range.

It was thought that if sodium chloride precipitates severe attacks of asthma, potassium chloride might produce the opposite effect, namely, reduction in the degree of severity of the asthma. This salt was therefore fed to the patient for a period of fifteen days. Starting with 5 Gm. per day, the amount was gradually increased to 25 Gm. During this period the child had much relief. In fact, it was considered to be one of her best periods. The asthmatic wheezing did not entirely disappear, but there was relatively little. The question arose whether this was a spontaneous remission, with no relation to the administration of the salt. The administration of potassium chloride was discontinued and sodium chloride was substituted. It was given for five days in large amounts, ranging from 25 to 40 Gm. per day. There was a quick flare-up in the asthma. The patient became very lll, and was so uncomforable that calcium chloride was given on the assumption that it would be more rapidly effective than potassium chloride in the reduction of the severity of the asthma. Large doses of the calcium salt were administered. The first day 5 Gm. was given, and this amount was increased to a maximum of 20 Gm., or 130 grains, per day. Administration of the salt was continued for seven days. There was little or no change in the asthma. This experience led us to give no consideration to calcium chloride in our future studies.

On referring again to chart 1, it will be noted that there was a gradual increase in the weight of the patient during the period of administration of potassium chloride. This gain continued through the subsequent short period during which sodium chloride was given. When calcium chloride was fed in large amounts the weight of the child began to decrease. The blood pressure was irregular during all the latter periods of observation. At no time was it unusually high or low.

Chart 2 reveals the changes which occurred in the blood serum during the sixty day period the patient was under observation. Placing the child on diet 1 was associated with a drop in the potassium, chloride and sodium in the blood serum. When large amounts of sodium chloride

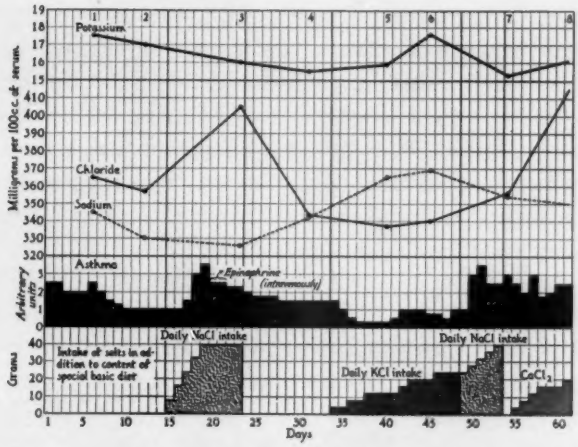

Chart 2.—Variations in the potassium, chloride and sodium of the blood serum in association with the low salt diet and the ingestion of large amounts of sodium chloride, potassium chloride and calcium chloride. The patient and the period of observation are the same as in chart 1.

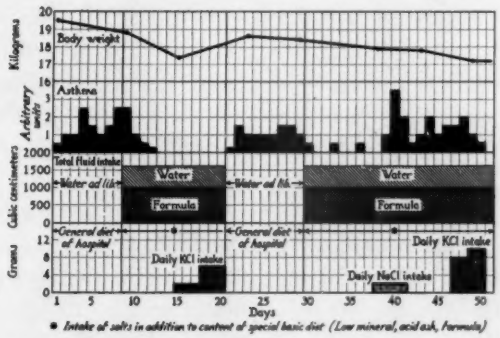

Chart 3.—Data from an investigation on D. B., a 4 year old boy with relatively mild but persistent asthma, showing the good response to diet 2, or the low mineral, acid ash formula and the elimination of the unfavorable results of giving sodium chloride by the administration of potassium chloride.

were added to the diet, the levels of potassium and sodium continued to drop. There was, however, an increase in the amount of chloride. During the period when potassium chloride was administered the chloride level dropped and the amounts of potassium and sodium in the

serum rose, the potassium reaching a high level toward the end of this period. The sodium level was highest when calcium chloride was given.

The second complete study was made on a 4 year old boy with bronchial asthma, and the data obtained are shown in chart 3. After an initial period of rest, with the patient receiving the general diet of the hospital, he was placed on diet 2, or the low mineral, acid ash formula, with a measured amount of water. The purpose of this was to observe whether a diet low in sodium chloride would influence the asthma. There was a loss in weight when this diet was employed. The asthma disappeared. Potassium chloride was then administered, starting with 2 Gm. and increasing to 6 Gm. This did not precipitate any attacks of asthma. The patient was returned to the general diet of the hospital, with no restriction on the intake of water and sodium chloride. Asthma appeared promptly and increased in severity throughout the time the child was on the hospital diet.

Nine days of this diet had apparently produced asthma sufficiently severe to warrant a return to the formula. When it was introduced the patient began to improve. Since the observations in the first study indicated that sodium chloride could produce an asthmatic attack, it was added to the formula. Only small amounts of the salt were employed. Two grams was given each day for four consecutive days. The result was a rather rapid increase in the severity of the asthma. After discontinuing the sodium chloride, potassium chloride was again administered; this time the amount was increased to 10 Gm. per day. There was a slow decrease in the asthmatic symptoms. When the administration of the potassium salt was discontinued the asthma disappeared rapidly.

Chart 4 gives a comprehensive picture of the results obtained during a most interesting period of observation on a 10 year old girl with bronchial asthma. During this time (a period of sixty days) she was watched closely. Throughout the period there was little variation in the blood pressure. Neither did the weight of the child show any significant changes except for the slight gains which occurred during the periods of increased intake of salt and indicated a shift in the hydration of the body. During the first ten days the patient was on the general diet of the hospital. After four days hyperpyrexia was instituted by means of the modified Simpson-Kettering machine. The temperature was gradually elevated to 40 C. (104 F.) and kept at this level for five hours. Then it was allowed to fall slowly to normal. There was some improvement in the asthma, but it did not continue long, and the next step was the placing of the child on the special basic formula, or diet 2. The intake of water was carefully controlled. The response to this diet was not the same as that of the patient for whom data are shown in chart 3.

On some days the child had little asthma; on other days there was an increase in the severity of the attack. Fever therapy was therefore again introduced in the same manner as in the first treatment. The response was rapid and favorable. In twenty-four hours the patient was entirely free of asthma and continued to remain so for many days. All this time the formula with the restricted intake of water was being given. The child felt fine and was up and about in her room. For the first time in many years she experienced the comfort of not having any difficulty in breathing.

Twelve days later sodium chloride was administered, starting with doses of 20 Gm. per day and increasing to 30 Gm. The salt was given for six days. Some asthmatic symptoms promptly appeared, but it was

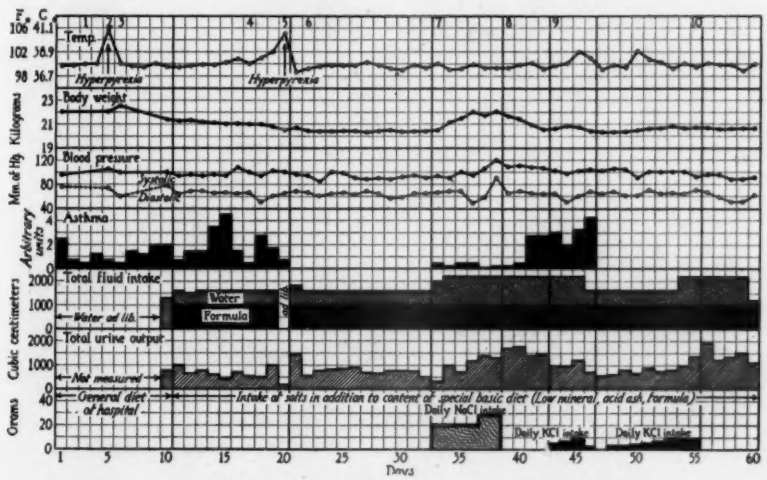

Chart 4.—Data obtained during an interesting period of study of M. L. M., a 10 year old girl with intractable asthma, revealing the influence of hyperpyrexia without and with the special low salt regimen, the sudden induction of a prolonged asthmatic attack by the ingestion of fairly large amounts of sodium chloride and the failure of potassium chloride to produce any asthma.

not until two days after the administration of sodium chloride had been discontinued that the attacks suddenly became much worse. Potassium chloride was then administered but the asthma was little influenced. In fact, it increased in severity. Administration of the salt was discontinued and immediately the asthma disappeared. This seemed to indicate that the potassium chloride had aggravated the asthmatic condition. To rule this out administration of the potassium salt was again started during the period when the child was free of asthma. Two grams was given the first day, and this was increased to 10 Gm. per day. Potassium

chloride was given for eight days, without producing an asthmatic attack. Five days later this study ended. The patient still did not have any signs of asthma.

The changes which occurred in the levels of potassium, chloride and sodium in the blood serum during the period of observation of the patient just cited are shown in chart 5. During the two periods of hyperpyrexia there was a marked rise in the level of serum potassium. This rise was of short duration. There was, however, a gradual increase in the amount of potassium for the first thirty days of the study. With the addition of sodium chloride to the diet the level of potassium dropped, rising again slowly during the periods when potassium chloride was administered.

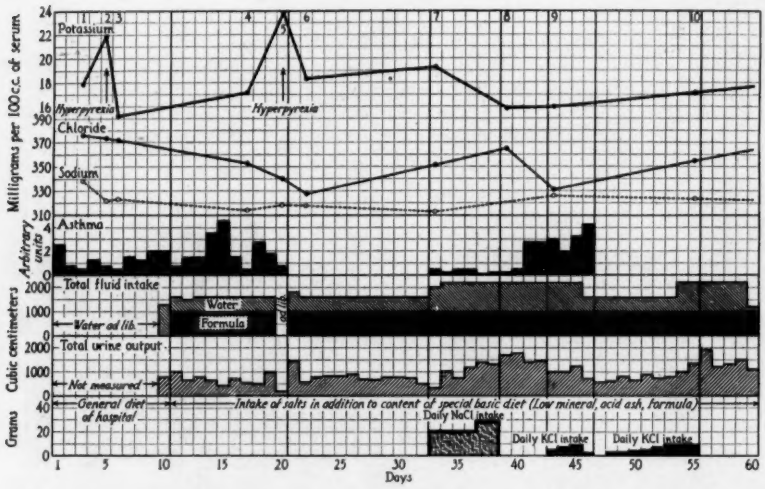

Chart 5.—Variations in the levels of potassium, chloride and sodium in the blood serum in connection with the various procedures used to affect the electrolyte exchange. The patient and the period of observation are the same as in chart 4.

The chloride level fell during the early periods of the investigation, that is, during the time that the fever therapy was given to the patient. After the second treatment, and during the period when the child had no asthma, the chloride was at its lowest level. The precipitation of the asthma with the administration of sodium chloride was associated with a rise in the serum chloride. This increase was not maintained, and when the potassium chloride was administered the first time the serum chloride was again at a lower level. From then to the end of the study the amount of chloride gradually increased. The level of serum sodium remained fairly constant throughout the entire sixty day period of the investigation.

In chart 6 are data on another child of whom a thorough study was made. This patient was a 12 year old boy who cooperated well. Since there were no significant changes in the blood pressure throughout the entire period of observation, a record of the readings was omitted from the chart. During the first few days of the study the patient was permitted to have the general diet of the hospital. Asthma was marked, and fever treatment was introduced. This period of hyperpyrexia was followed by diminution in the severity of the asthma, which continued for the remainder of the period during which the hospital diet was given. The only change in the levels of potassium, chloride and sodium in the

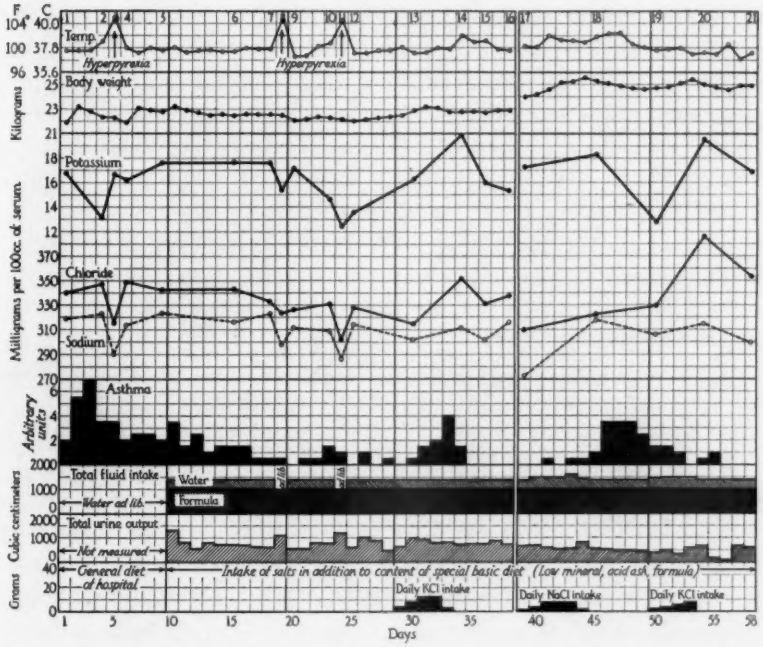

Chart 6.—Observations made during a period of thorough investigation on H. B., a 12 year old boy with severe intractable asthma, showing the failure of the special basic diet and hyperpyrexia to give a complete remission, the beneficial effect of small doses of potassium chloride and the precipitation of a severe attack of asthma lasting many days by administration of small amounts of sodium chloride.

blood serum was a temporary drop in association with the fever treatment.

The patient showed no signs of further improvement, and therefore he was placed on the special low mineral, acid ash formula. Gradually the asthmatic symptoms decreased, but did not entirely disappear. Another fever treatment was given. After this, the asthma was absent for one day and then it gradually reappeared. Therefore it was decided

to give a third period of hyperpyrexia. This treatment controlled the asthma but did not eliminate it. Each of the latter two fever treatments was followed by a slight dip in the levels of the potassium, chloride and sodium in the blood serum. After the last treatment the potassium did not return to the original value. However, at this time potassium chloride, in doses starting with 3 Gm. and increasing to 12 Gm., was administered in the hope that it might cause the complete disappearance of the asthma. Instead, the condition became worse, but a remission occurred after administration of the salt was discontinued. Meanwhile, the serum potassium had risen to the highest level observed during the study.

The child remained free of asthma for a long time. All this time he continued to take the special formula. He was allowed to be up and about. Activity, and even changes in weather, did not cause any asthma. Finally, sodium chloride, in doses beginning with 1 Gm. and increasing to 8 Gm., was added to the diet, with the result that some symptoms of asthma appeared, and because it was feared that longer administration of the sodium chloride might cause severe attacks of the disease it was discontinued. After this the asthma suddenly became much worse. Potassium chloride was again administered, in doses starting with 2 Gm. per day and increasing gradually to 8 Gm. There was some improvement during the period that the salt was given, but after it was discontinued the asthma disappeared. The child was active and comfortable for the remainder of the investigative period.

The level of serum potassium fell after the ingestion of sodium chloride but rose again when potassium chloride was given. The level of serum chloride changed little until after the administration of potassium chloride, when there was a sudden elevation, which was not maintained. There was an increase in the serum sodium during the administration of sodium chloride, and no further change occurred during the remainder of the study.

A review of the data presented in the charts shows that diet 1 did not influence greatly the asthma in the children studied. On the other hand, diet 2, or the low mineral, acid ash formula, led to disappearance of the asthma in 1 child and reduced it significantly in 2 others. Potassium chloride had a favorable influence on the asthma in the 1 child on diet 1, and administration of the salt appeared to be associated with the onset of remissions in 3 other instances. Hyperpyrexia or fever therapy was most effective in reducing the severity of asthma in the patients who were on the low mineral formula. Two children responded to this form of treatment fairly well.

In addition to the studies on the 4 children already mentioned, complete investigations were made on 8 other patients with intractable asthma. Four of the latter group were placed on the diet extremely low

in salt, with no change in the asthmatic condition. After about ten days of restriction of salt, fever therapy was introduced; complete remission of the asthma occurred in 3 patients and a striking reduction of symptoms in the fourth. The remaining 4 subjects also received the low mineral, acid ash formula. In these patients some decrease in the severity of the asthma was apparent when potassium chloride was administered in the usual manner, that is, beginning with small doses which were increased until the patients received somewhere between 6 to 10 Gm. of the salt daily. The 2 patients with less severe asthma gradually ceased wheezing, but the 2 with more severe attacks showed no change, neither aggravation nor improvement. However, the symptoms of these 2 patients stopped abruptly when administration of the salt was discontinued after four or five days.

COMMENT

The foregoing results afford ample proof that the mineral content of the diet is of importance in the control of bronchial asthma occurring in children. Although the first special basic diet (moderately low in sodium, potassium and chloride) which was employed caused no marked changes in the patients' asthma, there was a degree of improvement. The addition of large amounts of sodium chloride caused a rapid increase in the severity of the asthma. This type of response was obtained many times. It was especially apt to occur after the child had been on a diet low in salt for a limited period, with a corresponding decrease in the asthma; the sudden introduction of sodium chloride caused a quick upset. The high intake of sodium chloride made it difficult to control the asthma with the administration of epinephrine (1:1,000). On several occasions the drug had to be given intravenously. McQuarrie and others [2] observed the opposite effect in cases of diabetes mellitus. Increased ingestion of sodium chloride aided in the handling of their patients with small doses of insulin.

If the diet was made extremely low in sodium and potassium and the children were permitted to remain on this second diet or formula for a short period, the asthma gradually became less severe, in some cases disappearing almost entirely. The patients in whom the asthmatic symptoms did not disappear were subjected to artificial fever, induced by the Simpson-Kettering hypertherm. This form of therapy helped in reducing or eliminating the attacks when the children were continued on the diet extremely low in salt. It failed to give good results when the subjects were placed on the regular general diet of the hospital. The artificial hyperpyrexia caused further depletion of the sodium in the body. Keutmann, Bassett and Warren [11] have definitely demonstrated that there is a loss of sodium and chloride during the periods of artificial

11. Keutmann, E. H.; Bassett, S. H., and Warren, S. L.: Electrolyte Balances During Artificial Fever with Special Reference to Loss Through the Skin, J. Clin. Investigation **18**:239, 1939.

fever therapy if no salt water is administered during the procedure. The extremely low sodium content of the formula plus the administration of only distilled water during the fever treatment reduced the sodium ion concentration to a low level in the body. This condition was associated with disappearance of asthmatic symptoms.[12] Such a remission could easily be terminated by the addition of small amounts of sodium chloride. In practically every instance the asthma returned. In some cases the asthmatic symptoms were rather severe soon after the ingestion of the salt, and in others there was a gradual increase in the amount of asthma during the period of administration of sodium chloride, with a marked increase in symptoms after the salt was discontinued.

Much has been written concerning the relation between the sodium and potassium ions; therefore it was natural to wish to determine the effect of potassium chloride. Potassium chloride was administered to the children receiving the special diet low in sodium chloride. The patients with less severe attacks gradually ceased to have asthmatic symptoms, while the others showed little change. Prompt improvement, however, followed discontinuance of administration of the salt. This observation was interesting in view of the fact that this response was exactly the reverse of that obtained when sodium chloride was employed. The increase in the severity of the asthma in some children during the administration of potassium chloride suggested its use during periods when the patients had no asthma. No asthmatic symptoms appeared during or after its ingestion.

The beneficial effects of potassium chloride during its ingestion in children with a mild or moderate degree of asthma and after its discontinuance in those with severe asthma are hard to explain. The investigations of others offer little help. Camp and Higgins,[13] after reviewing the literature, carried out experiments on dogs in order to determine the specific action of potassium. They found that it was responsible for the typical changes ascribed to epinephrine. Of special interest was the observation that the constriction of the bronchi induced by histamine was relieved as promptly and completely by potassium as by epinephrine. Other investigators,[14] using the cat, opossum, rat and rabbit for their

12. Sheldon, J.; Howes, H., and Stuart, G.: Observations on Total Water and Sodium Exchanges in Asthmatic Patients, J. Allergy **11**:1, 1939.

13. Camp, W. J. R., and Higgins, J. A.: The Role of Potassium in Epinephrine Action, J. Pharmacol. & Exper. Therap. **57**:376, 1936.

14. D'Silva, J. L.: The Action of Adrenaline on Serum Potassium, J. Physiol. **86**:219, 1936. Larson, P. S., and Brewer, G.: On the Relation of Potassium to the Blood Pressure Response to Epinephrine, J. Pharmacol. & Exper. Therap. **61**: 213, 1937. Fenn, W. O.: The Potassium and Water Contents of Cat Nerves as Affected by Stimulation, J. Neurophysiol. **1**:1, 1938; Factors Affecting the Loss of Potassium from Stimulated Muscles, Am. J. Physiol. **124**:213, 1938. Wilde, W. S.: The Distribution of Potassium in the Cat After Intravascular Injection, J. Biol. Chem. **128**:309, 1939.

experiments, have procured results similar or closely related to those of Camp and Higgins.[13] Experiments have also been carried out on man by Brewer and his co-workers.[15] Whenever potassium has been employed in these studies it has been given intravenously as potassium chloride. The question whether these observations therefore explain the results obtained in our patients, to whom the potassium was administered orally, cannot be answered satisfactorily at this time. In the animal experiments, the changes in the serum electrolytes, especially potassium, were fairly constant in response to the intravenous administration of potassium chloride and the injection of epinephrine. In our children, who received the salt by mouth, this did not occur. When the results for each subject were compared, there were found marked variations in the levels of serum electrolytes in association with the ingestion of potassium chloride.

In spite of the lack of constant changes in serum potassium, which might be of scientific value, the oral administration of potassium chloride continues to give fairly good results in treatment of allergic diseases. Rusk and Kenamore[16] reported 6 cases of chronic urticaria in which definite improvement was attained by the use of a low sodium, high potassium, acid ash diet. Although Bloom[17] found potassium chloride of value in the treatment of hay fever and allergic rhinitis, he observed no appreciable effect on bronchial asthma. These patients had not been placed on a salt-poor diet. However, when both the potassium chloride and the low salt diet were employed, some of the patients with asthma were improved, but not cured. Abt[18] used potassium chloride in conjunction with a limited intake of sodium chloride and obtained similar results. While these clinical observations are encouraging in indicating the value of certain electrolytes, such as potassium, in the control of allergic disorders, especially asthma, they afford little help in revealing the underlying mechanism producing the beneficial response.

Kirstein and Bromberg[19] showed that the hyperglycemia which accompanies and follows fever therapy is due not to an increased concentration of blood constituents but to disturbances in carbohydrate

15. Brewer, G.; Larson, P. S., and Schroeder, A. R.: On the Effect of Epinephrine on Blood Potassium, Am. J. Physiol. **126**:708, 1939.

16. Rusk, H. A., and Kenamore, B. D.: Urticaria—A New Therapeutic Approach, Ann. Int. Med. **11**:1838, 1938.

17. Bloom, B.: The Use of Potassium Salts in Hay Fever, J. A. M. A. **111**: 2281 (Dec. 17) 1938. Bloom, B., and Grauman, S. J.: Potassium in Allergy, Southwestern Med. **23**:205, 1939.

18. Abt, A. F.: Note on Oral Administration of Potassium Chloride in Treatment of Hay Fever, Nasal Allergy, Asthma and Sinusitis, Am. J. M. Sc. **198**:229, 1939.

19. Kirstein, M. B., and Bromberg, L.: The Effect of Fever Therapy upon Carbohydrate Metabolism, J. Lab. & Clin. Med. **25**:7, 1939.

metabolism. Silvette and his co-workers [20] found that the injection of subtoxic amounts of potassium salts in animals resulted in a marked rise in blood sugar and decrease in glycogen in the liver, muscle and heart. It appears that an important effect of raising the level of potassium in the body is the production of glycogenolysis, or the inhibition of glycogen formation, and concomitant hyperglycemia. Early in our investigation, 3 [21] of the subjects ingested large amounts of dextrose and also received dextrose intravenously. There was a favorable influence on the asthma in each instance. Later, these asthmatic children responded satisfactorily to the administration of potassium chloride.

Recently Rusk, Weichselbaum and Somogyi [22] have performed experiments which indicate that in man there may be a more or less consistent rise of the serum potassium during an acute attack of an allergic disease such as asthma, and that with the subsidence of clinical symptoms the potassium content of the blood falls. Because of the well established fact that most of the potassium in the body is stored inside the cells, this increase of potassium in the blood serum may indicate a loss of this electrolyte from the cells, which in turn favors a prolongation of the undesirable allergic manifestations. There is preliminary evidence [23] that potassium lost from cells, such as those of muscle, is taken up in part by the liver. The ingestion of potassium in some form liberates the potassium from the liver and restores it to the muscle cells. However, additional evidence is needed before the existence of such a cycle can be stressed.

Bloom [17] referred to the importance of altered electrolyte metabolism in endocrine disturbances and suggested that allergy is basically an endocrine dysfunction, with secondary changes in the electrolyte metabolism. The Pottengers [24] have used a crude extract of the adrenal cortex in the treatment of asthma. Their results tend to show that the adrenal gland is primarily involved. Marenzi [25] performed experiments on dogs which strongly support the hypothesis that the adrenal cortex hormone is a factor which regulates the fixation of potassium in tissues, its

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20. Silvette, H.; Britton, S. W., and Kline, R.: Carbohydrate Changes in Various Animals Following Potassium Administration, Am. J. Physiol. **122**:524, 1938.

21. Stoesser, A. V., and Cook, M. M.: Hypertonic Dextrose Solutions in the Treatment of Bronchial Asthma, Journal-Lancet **58**:12, 1938.

22. Rusk, H. A.; Weichselbaum, T. E., and Somogyi, M.: Changes in Serum Potassium in Certain Allergic States, J. A. M. A. **112**:2395 (June 10) 1939.

23. Potassium in Muscle, editorial, J. A. M. A. **113**:1571 (Oct. 21) 1939.

24. Pottenger, F. M., Jr., and Pottenger, F. M.: Adrenal Cortex in Treating Childhood Asthma: Clinical Evaluation of Its Use, California & West. Med. **49**: 271, 1938.

25. Marenzi, A. D.: Blood Potassium and Suprarenal Glands, Endocrinology **23**:330, 1938.

urinary excretion and its equilibrium between plasma and tissues and that epinephrine is a factor in the rapid mobilization of potassium in the liver. These observations again associate the potassium ion with the control of allergic diseases and make it necessary to include potassium with other electrolytes, such as sodium, which is being investigated by Sheldon,[12] in any studies involving a determination of the fundamental or underlying mechanism of asthma. More intensive investigations, including studies of the water and electrolyte exchanges and the serum acid-base balance, are indicated. They have already been started in that the urinary and fecal excretions collected during the special periods of observation on the asthmatic children discussed in this report have been analyzed for their mineral constituents. The results will be compiled and presented in a future communication.

SUMMARY

Twelve children and young adults with asthma which proved intractable under routine allergic management were observed under the standard metabolic conditions customary in pediatric wards. Various procedures which affect the electrolyte exchange were instituted.

Two patients with persistent asthma were given the general diet of the hospital with no restriction of salt. When they received artificial fever no lasting improvement in the asthmatic symptoms occurred. After this, these 2 subjects and 4 others were placed on a diet extremely low in salt, with continuation of the asthma in spite of the restriction of salt. However, after ten days, when artificial fever treatment was instituted, a complete remission occurred in 5 patients and a striking reduction of symptoms in the sixth.

Three children with less severe asthma did respond to the regimen of salt restriction. The asthma disappeared completely in 1 patient, and its severity was reduced significantly in the 2 others.

The entire group of 9 patients who experienced cessation of asthmatic attacks while on the diet low in salt, with or without fever therapy, were maintained in *status quo* for a short period. Then they were given sodium chloride by mouth. In all cases the asthma reappeared and continued to grow worse even after addition of the salt was discontinued.

Four of the subjects in whom an attack of asthma was precipitated by the administration of sodium chloride and 4 more patients, all of whom were on the diet low in salt, with no abatement of the asthmatic symptoms, were then given potassium chloride by mouth. This salt had a favorable influence on the asthma in 6 patients, but in the remaining 2 subjects, who had rather severe asthma, there was no change. The symptoms stopped abruptly, however, when the administration of potassium chloride was discontinued.

Three children who were on the low salt diet and in a state of remission were given potassium chloride in order to observe whether administration of the salt could induce an attack of asthma. In no case were any symptoms evident during the administration of the salt or afterward.

In all cases variations in the salt metabolism were associated with corresponding changes in the hydration of the body, reflected by alterations in weight. There were no significant changes in the blood pressure.

Studies were made on the blood of 5 children, but no consistent changes in the levels of potassium, chloride and sodium in the serum were obtained in association with the various procedures which affected the electrolyte metabolism. The results of determinations on the blood of 3 patients were indicated graphically in charts 2, 5 and 6.

A review of the literature did not disclose any experiments which could definitely explain the beneficial effect of either depletion of salt (sodium chloride) in the body or the administration of potassium chloride. However, fundamental studies by several investigators now in progress suggest that the changes in the electrolytes influence asthma because they have a definite connection with neurogenic and endocrine functions.

CONCLUSIONS

Repeated observations on the 12 patients warrant the following conclusions, which are subject to change, depending on the results obtained from our present studies involving water balance, mineral metabolism and acid-base equilibrium of the serum.

1. Artificial fever gives only transient benefit in asthmatic patients whose intake of sodium chloride is normal or high before and during treatment.

2. Fever therapy gives striking improvement or complete remission in asthmatic patients on a continuous special diet low in salt (at least below 200 mg. of sodium daily).

3. Remissions due to the low intake of salt plus artificial fever can be terminated promptly by adding as little as 1 to 2 Gm. of sodium chloride to the diet.

4. The addition of potassium chloride (6 to 10 Gm. daily) to the special diet low in salt causes cessation of the milder attacks of asthma. The more severe asthma continues while potassium chloride is taken but ceases at once when administration of the salt is discontinued.

5. Potassium chloride (6 to 10 Gm. daily) given to patients during remissions does not cause the recurrence of asthma.

PROPHYLAXIS AND TREATMENT OF WHOOPING COUGH WITH A PERTUSSIS ANTIGEN

REPORT OF RESULTS

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The first accurate description of whooping cough was given by de Baillou [1] in 1578, and yet in 1939 the multiplicity of remedies recommended for the treatment of this disease is an index of therapeutic failure. Among the various remedies recommended in the recent literature as helpful in the treatment of pertussis are: ascorbic acid,[2] an endotoxin,[3] a pertussis antigen, administered intranasally,[4] and convalescent serum,[5] to say nothing of the vast amount of vaccines being sold and the many sedatives prescribed.

While there is at present no adequate or specific treatment for whooping cough, progress has been made in the prophylaxis of this disease by the development of the Sauer vaccine.[6] There were 42,655 deaths in the United States occurring in six consecutive years from whooping cough. This mortality is greater than that from diphtheria, scarlet fever, measles or tuberculosis. It has also been shown that in London 44 per cent of the children have had pertussis before their fifth birthday and 60 per cent before their tenth year, while in the United States 78 per cent of all adults have had the disease.

The antigen used was manufactured by Lederle Laboratories, Inc.

From the Department of Pediatrics, University of Maryland School of Medicine and College of Physicians and Surgeons.

1. Baillou, cited by Sauer, L. W.: Whooping Cough, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 2, chap. 34, p. 1.

2. Armerod, M. J., and Unkauf, B. M.: Ascorbic Acid (Vitamin C) Treatment of Whooping-Cough, Canad. M. A. J. **37**:134 (Aug.) 1937.

3. Thompson, A. R.: Pertussis Endotoxin in the Treatment of Whooping-Cough, Lancet **2**:733 (Sept. 25) 1937.

4. Schooten, S. S.: Intranasal Administration of a Pertussis Antigen, J. Michigan M. Soc. **36**:849 (Nov.) 1937.

5. Meader, F. M.: Prophylaxis of Whooping Cough, Am. J. Dis. Child. **53**:760 (March) 1937.

6. Sauer, L.: Prevention and Treatment of Whooping Cough, Pennsylvania M. J. **41**:177 (Dec.) 1937.

In view of these facts, a study was instituted to determine the value of a new pertussis antigen recommended for the treatment of this disease. Since this study was instituted, varying reports have been received concerning the value of pertussis antigen. Greenstein and Levy [7] observed no effect from the antigen. Our results with similar doses (0.5, 0.8 and 1.0 cc.) were likewise disappointing; but when the amount was increased to an initial dose of 1.5 cc. results were more encouraging.

Pertussis antigen (detoxified) is made from the growth of selected toxic and antigenic cultures of Haemophilus pertussis in an especially prepared beef heart infusion broth. The cultures used cause necrotic areas on intradermal injection in rabbits; they give an agglutinating serum with a titer of 10,000 to 20,000, which also has a high complement fixation titer, and they produce an antitoxin, as shown by tests in vivo. The cultures are carried on agar containing 30 per cent blood, which insures a continuance of phase 1 in the culture over relatively long periods.

These antigenic cultures are planted into the broth and grown for four days under conditions favorable for production of toxin. The bacterial growth is then removed in the Sharples centrifuge and the toxic filtrate separated in the Berkefeld filter. Samples are then taken for tests of toxicity and the remainder treated with a solution of formaldehyde to give a final concentration of 0.1 per cent. The detoxification is completed in four days at 40 C.

The toxicity of every batch is tested on mice and rabbits. Intradermal injections of the undiluted toxin into rabbits give a necrotic area about 20 by 20 mm., which is usually read as a 3 plus or a 4 plus necrosis. The lethal quality for mice is tested by making various dilutions of the toxin and injecting 0.5 cc. of each dilution intravenously into a series of mice. Ordinarily, the dilution containing from 0.1 to 0.15 cc. of toxin in a volume of 0.5 cc. kills all the mice in from twenty-four to forty-eight hours. The detoxified toxin does not produce necrosis when injected intradermally into susceptible rabbits and has no lethal effect on mice.

We are reporting our results with this antigen in the full knowledge that it is difficult to evaluate the results of any treatment in view of the great variation in the severity and duration of the disease. Since we had no standard on which to base our therapy, it was necessary to determine the optimum dose of the antigen per injection and the most advantageous time interval between doses, as well as the total amount of antigen which should be given. The study was divided into three sections: first, the effect of the antigen in the treatment of active pertussis;

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7. Greenstein, N. M., and Levy, W.: Treatment of Pertussis with a Detoxified Antigen, Am. J. Dis. Child. **59**:516 (March) 1940.

second, the immunizing effect of the antigen when administered as a routine to well infants and children; third, the influence of the antigen on children who had been exposed to pertussis but in whom there had not been sufficient time for the disease to develop fully.

Table 1 shows the number of patients with pertussis treated and the average duration of the attack. The average duration as recorded for 1,051 patients was three and fifteen-hundredths weeks. There was no appreciable difference between the results of treatment with antigen in the private and the dispensary patients.

TABLE 1.—*Duration of Attack in Patients Treated with Antigen*

	Number of Patients	Average Duration Before Treatment, Weeks	Average Duration After Beginning Treatment, Weeks	Average Total Duration, Weeks
Clinic patients	801	1.6	1.4	3.0
Private patients	250	1.5	1.8	3.3
Total	1,051	1.55	1.6	3.15

TABLE 2.—*Duration of Attack in Controls*

	Number of Patients	Average Duration Before Treatment, Weeks	Average Duration After Beginning Treatment, Weeks	Average Total Duration, Weeks
Group A *	76	2.3	3.0	5.3
Group B †	140	1.6	3.1	4.7
Total	216	1.9	3.05	5.0

* Patients treated either symptomatically or with a vaccine.
† Patients treated with a combined vaccine and antigen.

Table 2 consists of data for two control groups (A and B). It is of interest to note: first, that the duration after starting treatment was practically the same in both control groups, that is, three and five-hundredths weeks and, second, that the average duration after starting treatment in the patients given antigen, as reported in table 1, was approximately one half that of the controls, that is one and six-tenths weeks.

Table 3 lists the complications occurring in the patients treated with antigen, both before and after instituting treatment, as well as the complications occurring in the patients not treated with antigen. Complications occurred in 0.66 per cent of the patients given antigen, as compared with 18 per cent of the patients not treated with antigen. Also, there were 2 deaths, both of infants under 1 year of age, in the group not treated with antigen, while in the much larger group treated

with antigen there were no deaths. One infant treated with the antigen weighed but 11 pounds (5 Kg.) yet came through the attack successfully. (This child was exposed to both the brother and the sister, who had whooping cough.) Children of group B, consisting of 140 children who received the combined antigen and vaccine, are included in the group treated with antigen and did not show any complications.

Table 4 records data for 25 patients with pertussis in a small community with intimate cross contacts. Twenty patients of this group were given the antigen. Seventeen responded favorably; 3 showed no

TABLE 3.—*Incidence of Complications*

Among 1,051 Patients * Treated with Antigen		Among 76 Patients † Not Treated with Antigen
Before Instituting Treatment	After Instituting Treatment	
Bronchitis..... 2	Bronchitis..... 3	Pneumonia..... 2
Conjunctival hemorrhage 4	Conjunctival hemorrhage 1	Bronchitis..... 6
Otitis media..... 1	Otitis media..... 3	Chronic bronchitis..... 3
		Convulsions..... 1
		Deaths..... 2

* In 0.66 per cent.
† In 18.0 per cent.

TABLE 4.—*Data for Twenty-Five Patients with Pertussis in a Small Community with Intimate Cross Contacts*

	Treated	With Refractory Condition *	Untreated †
Number of patients.....	20	3	5
Average duration of illness.....	2.4 weeks	4 weeks	4 weeks
Complications.....	0	0	Otitis media..... 1
			Bronchitis..... 5
			Chronic bronchitis.. 3

* No satisfactory response occurred within two weeks.
† These patients were not treated with antigen because the parents objected.

response. The duration of the disease in the 17 patients averaged two and four-tenths weeks, as compared with four weeks for the patients whose condition was refractory and in those not treated with antigen. Of even more interest are the complications occurring in these 25 patients. No complications occurred in those receiving antigen, even though the duration of the attack was not shortened in the patients whose condition was refractory, while relatively many complications occurred in the patients not treated with the antigen. The average age of the 25 patients was 14 months.

Table 5 is of interest because it shows modification of an attack in an infant, 6 months of age, when the antigen was given. The disease developed in the same family in the older sister, mother and grandmother, as well as in a cousin. The cousin, who likewise had had the

antigen, had an attack of much shorter duration than the 3 members of the family not receiving it. The duration of the attack in the 2 children receiving the antigen was two weeks and three and a half weeks, as compared to seven weeks, eight weeks and five weeks in the 3 persons not receiving the antigen. Table 5 is interesting, also, because it shows

TABLE 5.—*Data on Pertussis in a Community* of Seven Related Families*

Patient	Relation to Doris	Age	Antigen †	Duration of Illness, Weeks
Doris (who had primary case).....		10 yr.	—	7.0
Irving.....	Brother	6 mo.	+	2.0
Patricia.....	Cousin	7 yr.	+	3.5
Florence.....	Mother	30 yr.	—	8.0
Florence.....	Grandmother	60 yr.	—	5.0
	Immunization			
Jessie.....	Cousin	14 mo.	Escaped	
Toni.....	Cousin	2 yr.	Escaped	
Bud.....	Cousin	7 yr.	Escaped	

* Total population: 18 adults and 6 children.
† Antigen given, +; not given, —.

TABLE 6.—*Dosage of Antigen*

Average Amount of Antigen per Dose *	Average Number of Injections	Average Total Amount of Antigen
1.5 cc.	4	6.0 cc.

* Minimum dose per injection, 0.5 cc.; maximum, 2 cc.

TABLE 7.—*Response of Ninety Seven Patients to Varied Amounts of Antigen*

Amount of Antigen per Dose	Number of Patients	Patients Improved								Patients Unimproved	
		After 2d Dose		After 3d Dose		After 4th Dose		Total			
		No.	%	No.	%	No.	%	No.	%	No.	%
0.5 cc.	33	3	9	9	28	7	21	19	58	14	42
1.0 cc.	26	13	50	3	11	3	11	19	72	7	28
1.5 cc.	11	9	82	1	9	0	0	10	91	1	9
2.0 cc.	27	14	52	9	34	2	7	25	93	2	7
Total	97	39		22		12		73		24	

that the 3 cousins, aged 14 months, 2 years and 7 years, respectively, who were immunized with the antigen immediately after exposure, escaped the disease, although they continued to be exposed throughout the outbreak.

Table 6 shows that the average amount of antigen given per dose was 1.5 cc., and the average number of doses was four.

Table 7 gives a clear picture of the effects of varying amounts of the antigen. Results depend largely on the amount of antigen given

per dose, and beyond a certain point additional antigen is of little value. There was a response after the second dose of 0.5 cc. in only 9 per cent of the patients receiving this dose, while there was a response after the second injection of 1.5 cc. in 82 per cent of the patients receiving this dose. When a larger dose, 2 cc., was given, the greatest response followed more equally the second and the third injections. The consistent increase of response corresponding to the increased amount of antigen given per dose is striking. Thus, when 0.5 cc. of the antigen

TABLE 8.—*Response to Varied Intervals Between Doses*

Interval in Days	Number of Patients	Patients Improved								Patients Unimproved	
		After 2d Dose		After 3d Dose		After 4th Dose		Total			
		No.	%	No.	%	No.	%	No.	%	No.	%
2	18	7	39	3	17	5	27	15	83	3	17
3	28	15	53	6	22	2	7	23	82	5	18
4	38	9	24	9	24	6	15	24	63	14	37
5	30	11	36	8	27	3	10	22	73	8	27
Total	114	42		26		16		84		30	

TABLE 9.—*Prophylactic Immunization* *

Number of Children Immunized	Number Definitely Exposed	Number Contracting Disease	Number Escaping Disease	Average Rate of Protection
982	183	34	149	81%

* The patients immunized have not been observed over a sufficiently long period to determine the duration of protection.

TABLE 10.—*Immunization After Exposure*

Number of Children Exposed	Number Escaping Disease	Number Contracting Disease	Rate of Protection
118	90	28	76%

was given, after four injections there was a response in only 58 per cent of the patients. When 1.0 cc. of antigen was given, the percentage of patients who showed a response increased to 72; and when the dose was increased to 1.5 cc., there was a response in 91 per cent of the patients after four injections. Further increasing the dose of antigen to 2 cc. caused an increase only to 93 per cent. The number of patients showing no response to the antigen likewise decreased from 42 per cent when 0.5 cc. was given to 7 per cent when 2 cc. was given. It seems advisable to give the maximal amount of antigen in the first injection

rather than increasing the dose subsequently. The majority of patients receiving 0.5 cc. in their first dose later were given 1 cc. The optimal amount of antigen per dose thus seems to be between 1.5 and 2 cc.

Table 8 indicates the optimum interval between doses. It appears that an injection should be given every second or third day for optimal results, there having been a response in 82 per cent of the patients after a total of four doses when the time interval was three days between doses, compared to a response in only 63 per cent when the time interval was four days. There was a response after the second dose at three day intervals in 53 per cent of the patients, while there was a response after the second dose at four day intervals in only 24 per cent, nearly 50 per cent less. Results were poorest from treatment at four day intervals, and lengthening the interval beyond this is not helpful in shortening the duration of the attack. The interval between doses, while important, does not seem as important as the amount of antigen given per dose.

Table 9 shows the results from prophylactic immunization and is self explanatory. The duration of immunity varied from five months to two and a half years. It is of interest to note that a number of infants immunized during this study with a mixed vaccine and antigen did not show any appreciable rate of protection.

Table 10 gives the results of immunization after exposure. Of 118 children exposed, 90 escaped pertussis, while 28 contracted the disease.

COMMENT

Twenty patients of the 1,051 treated did not show any response to the antigen; on the contrary, they had severe pertussis.

In this series, reactions from the antigen were unusual. Occasionally, one noted a slight rise in temperature lasting twenty-four hours or a slight redness of the arm. Three patients had an urticarial reaction.

Ages varied from 1 month to 10 years, the average age being 3 years. It is interesting to note, though, that 30 per cent of our patients were under 1 year of age.

Thirteen patients in whom the injections were prematurely stopped because of failure to return showed regression with progression of symptoms. In 6 of these patients there was a sluggish response to additional injections.

Children immunized with 6 cc. of antigen who had definite exposures showed a rate of protection of 94 per cent. In contrast among the rest of the patients, including 200 children immunized with only 3 cc. of the antigen, the majority, or 75 per cent, of the cases of pertussis developed.

SUMMARY

The antigen used apparently helped in the treatment of pertussis when administered early by reducing the incidence of complications and by shortening the duration of the attack.

Results, however, varied with the amount of antigen given per dose and the interval between doses.

The condition of a few patients in this series was refractory.

The antigen also appeared to offer a considerable degree of protection in the prophylaxis of pertussis, both before and after exposure.

ORAL AND INTRAVENOUS DEXTROSE TOLERANCE TESTS IN CASES OF ACUTE (CATARRHAL) HEPATITIS

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Various tests of hepatic function have been used in an attempt to evaluate the extent of damage of diseased livers, to determine prognosis in hepatic disorders and to aid in differential diagnosis.[1] No single test has yet been found which is entirely without defect.

The dextrose tolerance test has been used by some investigators as an aid in the differential diagnosis of jaundice and by others as an index of the degree of hepatic damage. Jacobi [2] reported on the results of oral dextrose tolerance tests in 25 patients with acute hepatitis, in 14 of whom the disorder was due to catarrhal icterus. In all these patients either a flat curve or a curve showing an early high rise with a fall to normal in two hours was obtained. Jacobi advised against surgical intervention when either type of curve was found. Shay and Fieman [3] obtained somewhat similar results in their cases of toxic hepatitis but stated the belief that more experience with the test was necessary before its usefulness could be definitely established.

Coller and Jackson [4] used the oral dextrose tolerance test to determine the function in carbohydrate metabolism of damaged livers of patients with disease of the gallbladder. They found that many of their patients had abnormal curves. After operative procedures had been carried out the dextrose tolerance returned to normal, and they concluded that the test was valuable in determining the function of the

From the Department of Pediatrics, University of Chicago.

1. Soffer, L. S.: Present Day Status of Liver Function Tests, Medicine **14**:185, 1935. Snell, A. M., and Magath, T. B.: The Use and Interpretation of Tests for Liver Function, J. A. M. A. **110**:167 (Jan. 15) 1938.

2. Jacobi, H. G.: (*a*) Glucose Tolerance as a Diagnostic Aid in Jaundice, Surg., Gynec. & Obst. **63**:293, 1936; (*b*) Glucose Tolerance as a Diagnostic Aid in Jaundice: II. Further Differentiation of Cases Showing an Obstructive Type of Curve, ibid. **64**:995, 1937.

3. Shay, H., and Fieman, P.: The Value of a Combined Study of the Newer Laboratory Tests in the Differential Diagnosis of Toxic and Obstructive Jaundice Including Blood Phosphatase, Cholesterol Partition, Galactose Tolerance and Glucose Tolerance, Am. J. Digest. Dis. **5**:597, 1938.

4. Coller, F. A., and Jackson, H. C.: Surgical Aspects of Hypoglycemia Associated with Damage to the Liver, J. A. M. A. **112**:128 (Jan. 14) 1939.

liver in carbohydrate metabolism. Wilson [5] observed improvement in the results of intravenous dextrose tolerance tests in 2 patients with acute hepatitis who had received liver extract and stated that the test could be used as an index of hepatic function.

Dextrose tolerance is usually measured by the determination of the blood sugar at various periods after the oral administration of a certain amount of dextrose. Several factors, not the least of which is the variable rate of absorption of dextrose from the intestine, make the interpretation of the oral dextrose tolerance test difficult. To eliminate this factor, the intravenous dextrose tolerance test has been advocated.[6] Both the oral and the intravenous dextrose tolerance test have been used serially for children with catarrhal jaundice in an attempt to answer the following questions:

1. Are the tests of any value in estimating hepatic function?

2. Are the types of curves obtained valuable in the differential diagnosis of the many forms of jaundice?

METHOD

The children were made to fast from fourteen to sixteen hours prior to each test. The intake of water was not restricted. The intravenous dextrose tolerance test was performed first, and on the following day the oral test was done. In a small percentage of the patients this order was not followed. In the intravenous test, 0.5 Gm. of dextrose per kilogram of body weight (as a 20 per cent solution in a physiologic solution of sodium chloride) was injected into the antecubital vein. The time consumed by this procedure varied from three to five minutes. Specimens of blood were obtained by capillary puncture during fasting and two, fifteen, thirty, forty-five, sixty, seventy-five and ninety minutes after injection of dextrose. The dextrose tolerance to orally administered dextrose was determined after the ingestion of 1.75 Gm. of dextrose per kilogram. Specimens of blood were taken during fasting and one-half, one, two and three hours after ingestion of dextrose.

Blood sugar was determined by the micromethod of Folin.[7]

The icteric index was determined on venous blood (normal, 3 to 5 units).

The van den Bergh reaction and the amount of serum bilirubin were obtained according to the original method. (Normal content of serum bilirubin is 0.25 mg. or less per hundred cubic centimeters.)

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5. Wilson, R.: Intravenous Glucose Tolerance Curve as an Index of Liver Function and Liver Replacement Therapy in Cases of Hepatic Insufficiency, Canad. M. A. J. **40**:268, 1939.

6. (*a*) McKean, R. M.; Myers, G. B., and Von der Heide, E. C.: Blood Glucose Tolerance: Its Determination by a Micro-Interval Method; I. Studies on Normal and Diabetic Persons, Am. J. M. Sc. **189**:702, 1935. (*b*) Crawford, T.: A Standard Intravenous Glucose Tolerance Test, Arch. Dis. Childhood **13**:69, 1938. (*c*) Tunbridge, R. E., and Allibone, E. C.: The Intravenous Glucose Tolerance Test, Quart. J. Med. **9**:11, 1940

7. Folin, O.: A New Blood Sugar Method, J. Biol. Chem. **77**:421, 1928.

The content of total cholesterol was determined by the method of Bloor [8] (normal, 160 to 200 mg. per hundred cubic centimeters) and of cholesterol esters by the method of Bloor and Knudson.[9]

RESULTS

The tolerance to dextrose administered intravenously was considered decreased if the blood sugar of the one hour specimen was above 100 mg. per hundred cubic centimeters and increased if the blood sugar of the thirty minute sample was below that level. These figures have been arrived at from results of tests performed on normal children. Tolerance to orally administered dextrose was considered decreased if the blood sugar curve rose above 200 mg. per hundred cubic centimeters or if the blood sugar of the two hour specimen was above 100 mg. per hundred cubic centimeters. The interpretation of the "flat" type of curve is difficult, since decreased absorption of dextrose from the intestine or increased tolerance may be involved. In table 2, this type of curve is called "flat" rather than increased.

From a summary of the results obtained for 12 children with catarrhal jaundice (tables 1 and 2), there appears to be no close correlation between the type of curve obtained from either the oral or the intravenous administration of dextrose and the degree of jaundice (charts 1 and 2). Both the icteric index and the serum bilirubin content were used to measure the intensity of the jaundice. Determination of the icteric index proved to be a simple and valuable method, since a close degree of correlation was found between the icteric index and the bilirubin content of the blood (chart 3). Normal response to both oral and intravenous administration of dextrose was obtained in some instances when the icterus was deep, and decreased tolerance was found in other patients with low icteric indexes. In the individual patient, however, improvement in the tolerance to dextrose usually accompanied the decrease in jaundice and clinical improvement. When the tolerance to intravenously administered dextrose was found decreased, the tolerance to dextrose administered orally was similarly decreased. On the other hand, many of the patients had a normal response to intravenously injected dextrose but a definite decrease in tolerance to dextrose as measured by the oral method.

The determination of total cholesterol and of the percentage of cholesterol esters [10] was of some value. The values for total cholesterol were normal or below in all but 3 of the patients. The percentage of

8. Bloor, W. R.: The Determination of Cholesterol in Blood, J. Biol. Chem. **24**:227, 1916.

9. Bloor, W., and Knudson, A.: Determination of Cholesterol and Cholesterol Ester in Small Amounts of Blood, J. Biol. Chem. **27**:107, 1916.

10. Epstein, E. Z., and Greenspan, E. B.: Clinical Significance of the Cholesterol Partition of the Blood Plasma in Hepatic and Biliary Diseases, Arch. Int. Med. **58**:860 (Nov.) 1936.

TABLE 1.—*Summary of the Chemical Determinations on the Blood in Children with Catarrhal Jaundice*

Patient, Case Number	Sex and Age	Duration of Jaundice	Date	Icteric Index, Units	Serum Bilirubin, Mg./100 Cc.	Total Cholesterol, Mg./100 Cc. of Plasma	Cholesterol Ester, Percentage of Total	Comment
C. VanT. 1	Boy 10 yr.	12 days	10/29/38 11/ 6/38	28 19	2.2 (N)	165	18	Uneventful recovery; one of three members of family who had same disease
J. B. 2	Girl 5 yr.	4 mo.	12/ 4/38 12/16/38 12/27/38 1/ 3/39 1/ 9/39 1/20/39 2/ 8/39 3/ 3/39	120 140 110 70 50 40 30 20	8.9 11.4 4.5 2.9 1.5 (N) (N) (N)	191 168 171 161	70 42 46	Prolonged attack; ascites developed, which persisted for 18 days (12/25/38 to 1/12/39); transfusions given; blood chemistry normal; complete recovery
M. VanT. 3	Girl 14 yr.	7 days	1/ 4/39 1/25/39	.. ..	3.5 (N)	145	23	Two brothers also had catarrhal jaundice; uncomplicated recovery
N. B. 4	Girl 10½ yr.	15 days	1/23/39 2/ 1/39	.. ..	8.9 (N)	144	11	Intense icterus which cleared quickly; uncomplicated recovery
D. B. 5	Boy 8 yr.	10 days	4/26/39 5/ 3/39	64 6	8.0 (N)	139 167	63 33	Uneventful recovery
M. S. 6	Girl 5 yr.	14 days	10/31/39 11/ 7/39	21 11	2.0 1.4	186	31	Uneventful recovery
R. W. 7	Boy 14 yr.	1 mo.	12/12/39 12/18/39 12/19/39 12/22/39 1/ 2/40	45 .. 25 .. 12	5.5 ... 1.9 .... (N)	... 246 ... 183 168	.. .. .. 35 60	Two other members of family had catarrhal jaundice; uneventful recovery
J. J. 8	Girl 4 yr.	2 mo.	12/27/39 1/ 6/40 1/10/40 1/26/40 2/ 9/40	155 100 60 50 19	14 8.1 7.5 2.0 1.0	286	9	Treated for congenital syphilis; Wassermann reaction negative for past two years; had not received an arsenical preparation for two years; severe icterus but complete recovery
H. W. 9	Boy 7½ yr.	7 days	2/ 9/40 2/19/40	22 ..	1.9 ...	... 320	.. 13	Child was over acute symptoms when admitted; uncomplicated recovery
V. S. 10	Girl 6 yr.	9 days	2/29/40 3/ 8/40	25 7	2.2 (N)	...	..	Brother (F.S.) later contracted similar disease; uneventful recovery
S. C. 11	Boy 8 yr.	1 mo.	3/ 8/40 3/18/40 3/29/40	82 60 50	4.2 3.5 1.2	168	..	Mother also later had jaundice (nonobstructive); uneventful recovery
F. S. 12	Boy 7 yr.	7 days	4/ 6/40 4/15/40	17 9	2.3 0.4	115 128	26 57	Sister (V.S.) also had catarrhal jaundice; uneventful recovery

TABLE 2.—*Degree of Jaundice, Day of Illness and Type of Curves Obtained for Children with Catarrhal Jaundice in Oral and Intravenous Dextrose Tolerance Tests*

Case	Day of Admission	Intravenous Dextrose Tolerance Test				Oral Dextrose Tolerance Test			
		Days After Onset of Illness	Icteric Index	Dextrose Tolerance		Days After Onset of Illness	Icteric Index	Dextrose Tolerance	
C. VanT.	10/28/38	7	27	.....	Normal	6	26	Decreased	.....
1		..	..	.....	.....	9	20	.....	Normal
J. B.	12/ 2/38	49	120	Decreased	.....	38	135	Decreased	.....
2		84	45	.....	Normal	86	40	.....	"Flat"
M. VanT.	12/24/38	10	..	Decreased	.....	11	..	Decreased	.....
3									
N. B.	1/21/39	5	..	.....	Normal	4	..	Decreased	.....
4		12	..	.....	"Flat"	13	..	.....	Normal
D. B.	4/25/39	15	64	.....	Normal	16	64	.....	"Flat"
5		24	4	.....	"Flat"	29	4	.....	"Flat"
M. S.	10/18/39	13	..	Decreased	.....	14	..	Decreased	.....
6		19	..	.....	Normal	20	..	.....	Normal
R. W.	12/11/39	12	45	Decreased	.....	13	45	Decreased	.....
7		19	25	Decreased	.....	20	25	Decreased	.....
		34	12	.....	Normal	32	12	Decreased	.....
J. J.	12/21/39	6	155	.....	Normal	7	155	Decreased	.....
8		13	100	.....	Normal	14	100	Decreased	.....
		20	60	.....	Normal	21	60	.....	Normal
		34	50	.....	Normal	35	50	.....	Normal
H. W.	2/ 8/40	13	22	.....	Normal	14	22	Decreased	.....
9									
V. S.	2/29/40	2	26	Decreased	.....	3	26	Decreased	.....
10		9	8	.....	Normal	8	8	.....	Normal
S. C.	3/ 7/40	14	70	.....	Normal	12	82	.....	Normal
11									
F. S.	4/ 5/40	5	17	Decreased	.....	6	17	Decreased	.....
12		14	9	.....	Normal	15	9	Decreased	.....

esters was found to be below normal in 75 per cent of the patients. When the percentage of esters increased from the low values, clinical improvement and a decrease in the icteric index also occurred.

The duration of the jaundice varied from seven days in the acute form to four months in the prolonged type of the disease. Progress of all the patients is being followed, and no complications attributable to catarrhal jaundice [11] have been noted since discharge from the hospital.

COMMENT

The previous diet is one of the factors which may influence the oral dextrose tolerance test.[12] A high carbohydrate diet increases the toler-

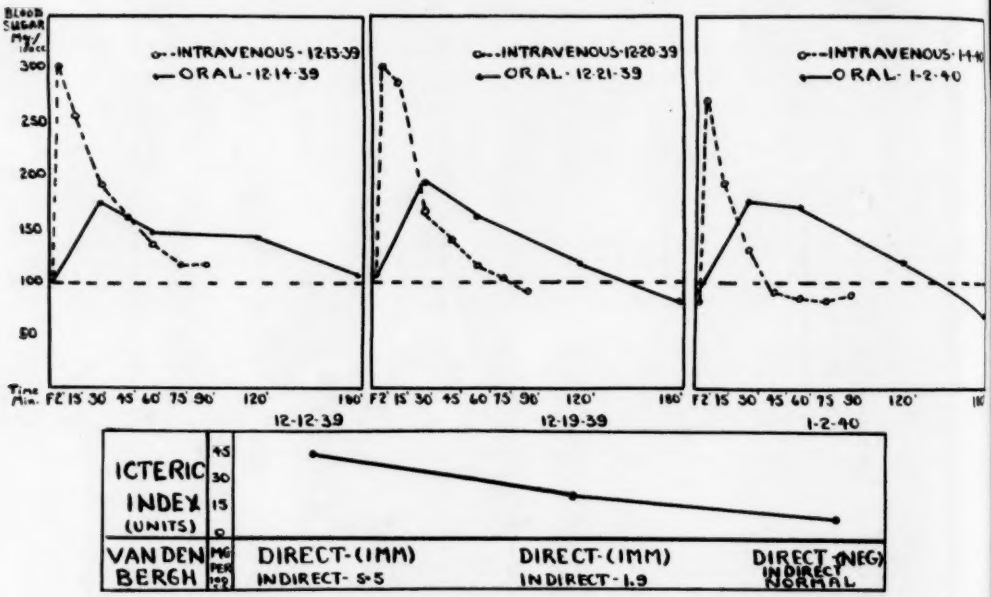

Chart 1.—Results of oral and intravenous dextrose tolerance tests and of determinations of the icteric index of a boy aged 14 years. Onset of the illness was on Dec. 1, 1939.

ance and starvation decreases it. During the early part of this work, 4 patients (cases 1, 2, 3 and 4) were given high carbohydrate, low fat diets, but the remaining children received average carbohydrate diets. The amount of carbohydrate used in the test was included in the total

11. Hurst, A. F., and Simpson, C. K.: Catarrhal Jaundice and Mild Hepatic Necrosis: Their Pathology and Diagnosis, Guy's Hosp. Rep. **84**:173, 1934. Ramhult, A.: Nodular Cirrhosis of the Liver After Acute Hepatitis, Svenska läk.-tidning. **35**:871, 1938; abstracted, Am. J. Dis. Child. **59**:426 (Feb.) 1940.

12. Himsworth, H. P.: Dietetic Factors Influencing Glucose Tolerance and Activity of Insulin, J. Physiol. **81**:29, 1934.

amount allowed for the day. If emesis had occurred, the test was delayed until the child had been free of this symptom for forty-eight hours.

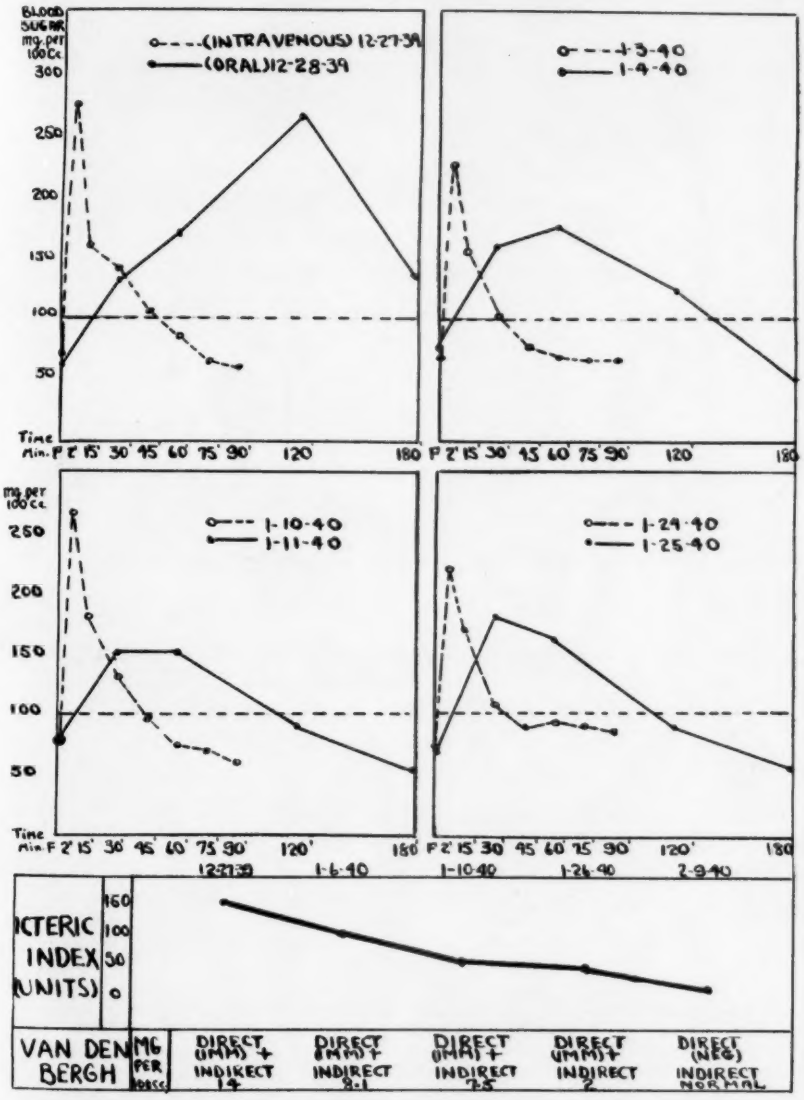

Chart 2.—Results of oral and intravenous dextrose tolerance tests and of determinations of the icteric index of a girl aged 5 years. Onset of the illness was on Dec. 21, 1939.

The type of diet apparently has some influence on the response to intravenously injected dextrose as well (McKean and associates [6a] and

Crawford [6b]). Two 9 year old children with nonactive orthopedic disorders were tested. Each received an average carbohydrate diet (carbohydrate, 200 Gm.; protein, 60 Gm.; fat, 90 Gm.) for one week, after which the intravenous dextrose tolerance test was done. The diet was

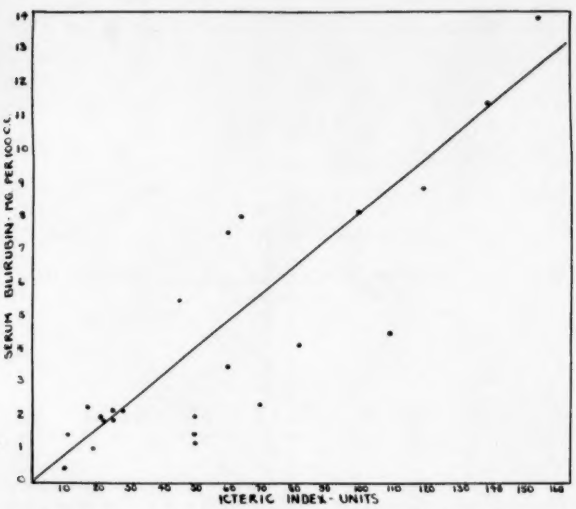

Chart 3.—Correlation between values for the icteric index and the bilirubin content of the blood.

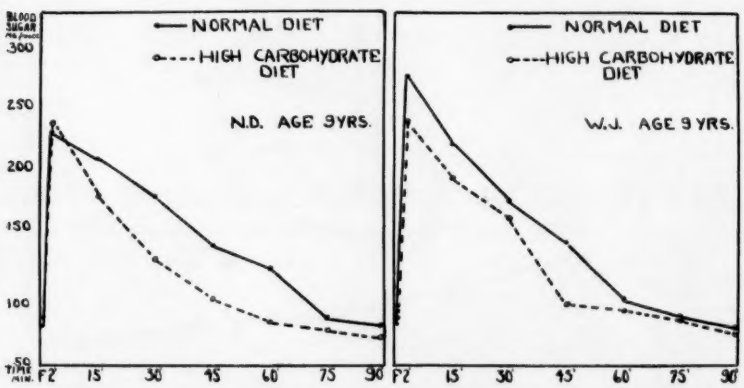

Chart 4.—Effect of the diet on the intravenous dextrose tolerance test.

then changed to one high in carbohydrate (carbohydrate, 390 Gm.; protein, 50 Gm.; fat, 10 Gm.), and seven days later an increase in the tolerance to intravenously administered dextrose was obtained in both children (chart 4).

When dextrose is given by mouth, an increase in the glycogen in the liver can be found after the blood sugar has returned to normal. The

increased glycogen in the liver, however, is not the only factor in reducing the blood sugar, since utilization and storage in the tissues, as well as the action of the endocrine glands, play an important part. Mann and Bollman [13] have shown that partially hepatectomized dogs had a reduced tolerance for dextrose. When the liver was entirely removed, hypoglycemia resulted and the animal died, although the muscles were found to have abundant glycogen. Althausen and Thoenes [14] damaged the livers of rabbits by the daily injection of small amounts of phosphorus. They found a progressive decrease in sugar tolerance, which they stated could be partially accounted for by the lack of deposition of glycogen in the liver. Soskin, Allweiss and Cohen [15] obtained normal dextrose tolerance curves in depancreatized dogs which had been given sufficient insulin and dextrose to maintain the blood sugar at a constant level. Hepatectomized dogs, however, which also received insulin and dextrose, yielded a diabetic curve when dextrose was given. Further experimental work added support to the belief that the intact and uninjured liver was necessary for a normal result from the dextrose tolerance test. [16] Other investigators, however, explain the mechanism of the normal dextrose tolerance curve on the basis of an increased secretion of insulin, which results in the rapid utilization and storage of dextrose.[17]

The fate of dextrose administered intravenously has not been definitely determined. Within a few minutes after injection, a fairly large percentage of the dextrose has disappeared from the blood stream. That it has not been changed to some other nonreducing substance, and has remained in the blood has been established by the work of Kurokawa.[18] The secretion of dextrose in the urine is not an important factor, since

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13. Mann, F. C., and Bollman, J. L.: Liver Function Tests, Arch. Path. **1**:681 (May) 1926.

14. Althausen, T. L., and Thoenes, E.: Influence on Carbohydrate Metabolism of Experimentally Induced Hepatic Changes: Phosphorus Poisoning, Arch. Int. Med. **50**:58 (July) 1932.

15. Soskin, S.; Allweiss, M. D., and Cohen, D. J.: Influence of the Pancreas and the Liver upon the Dextrose Tolerance Curve, Am. J. Physiol. **109**:155, 1934.

16. Soskin, S.; Essex, H. E.; Herrick, J. F., and Mann, F. C.: The Mechanism of Regulation of the Blood Sugar by the Liver, Am. J. Physiol. **124**:558, 1938.

17. Sweeney, J. S.: Dietary Factors That Influence the Dextrose Tolerance Test: A Preliminary Study, Arch. Int. Med. **40**:818 (Dec.) 1927. Ricketts, H. T.: Carbohydrate Tolerance After Protamine Insulin: Its Bearing on the Physiology of Insulin Secretion, J. Clin. Investigation **17**:795, 1938.

18. Kurokawa, T.: Ueber das Schicksal des infundierten Zuckers mit besonderer Berücksichtigung der Zuckerdufnahmefähigkeit der Gewebezellen: Verhalten des Gesamt-C des Blutes nach Glukoseinfusion, Tohoku J. Exper. Med. **10**:64, 1928.

only a small amount (0.2 to 2 Gm.) has been found in the urine of patients who were tested. The decrease in blood sugar cannot be attributed to rapid oxidation, since a rise in the respiratory quotient does not occur until the blood sugar has returned to near the normal level.[19] Folin, Trimble and Newman [20] have shown that the storage of dextrose as glycogen in the liver or muscles does not play an important role in the disappearance of excess sugar from the blood. Recent results on rats in this laboratory are in accord with these observations.[21] However, the amount of dextrose entering and leaving the liver after the intravenous administration of this substance has been determined by Soskin, Essex, Herrick and Mann.[16] They found that the liver stored dextrose during the first two hours, but the form in which the carbohydrate appeared in the liver was not determined.

The liver has been found to have the largest amount of dextrose of any of the body tissues.[22] Palmer,[22] however, was unable to find an increase in dextrose in the liver thirty minutes after the intravenous administration of large amounts of the material in rabbits. In view of the lack of appreciable amounts of dextrose or glycogen found in the liver after rapid intravenous injection and the results of Soskin and associates,[16] it would appear that the dextrose in the liver may occur as some other form of carbohydrate. The foregoing hypothesis would be consistent with the widely accepted belief that the most probable cause of the disappearance of intravenously injected sugar is rapid diffusion of that substance into the tissues.[6a]

In many of the children studied in this series, the tolerance to orally administered dextrose was decreased, while the result of the intravenous test, performed earlier, was normal. The explanation might be offered that in an acute process, such as catarrhal jaundice, the state of the liver might change within a short period. Abnormal results from oral and normal results from intravenous tests have also been found in children with the prolonged type of catarrhal jaundice (cases 7 and 8). Similar results have been obtained in 2 children on whom autopsies were performed, 1 of whom had cirrhosis of the liver and the other carcinoma of the liver (chart 5). Admittedly, the oral dextrose tolerance test is more physiologic than the intravenous, but no adequate explanation can

19. Ritlop, B.: Ueber die Wirkung des Insulins auf Kohlenhydratverbrennung und Energieumsatz in Tieren denen Kohlenhydrat beigebracht wurde, Biochem. Ztschr. **219**:277, 1930.

20. Folin, O.; Trimble, H. C., and Newman, L. H.: The Distribution and Recovery of Glucose Injected into Animals, J. Biol. Chem. **75**:263, 1927.

21. Pachman, D. J., and Seckel, H. P. G.: Unpublished data.

22. Palmer, W. W.: The Concentration of Dextrose in the Tissues of Normal and Diabetic Animals, J. Biol. Chem. **29**:79, 1917.

be given for the wide discrepancy between the results of the two tests. Of the two methods, the oral dextrose tolerance test yields more information concerning the function of the liver in carbohydrate metabolism.

Neither test can be used with any degree of confidence in the differential diagnosis of catarrhal jaundice, since the shape of the curve varies considerably in different patients and also varies in the same patient during the course of the disease. In only 1 child in this series (case 2) was the correct diagnosis doubtful at any time. In this patient edema of the extremities and ascites developed three weeks after admission. While this complication has been described in cases of catarrhal jaundice,[23] its occurrence is unusual and has been attributed to the disturbance in the mechanism of water balance in which the liver plays a

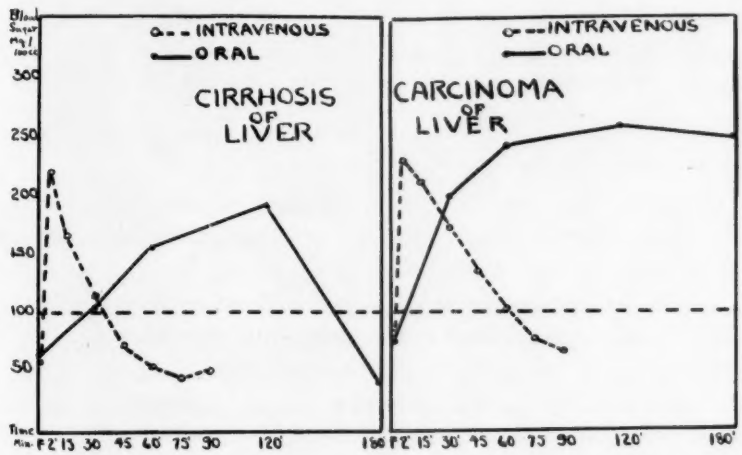

Chart 5.—Results of intravenous and oral dextrose tolerance tests in N. S., a patient with cirrhosis of the liver, aged 4 years, and in H. H., a patient with carcinoma of the liver, aged 6 years.

part.[23b] Normal values for serum albumin and globulin were found during the period of edema. The result of the oral dextrose test performed prior to the onset of edema was unlike either type of curve described as occurring in toxic hepatitis.[2a] The edema subsided spontaneously, and the child had an uneventful, though prolonged convalesence.

That the liver has an important role in the maintenance of a normal blood sugar seems definitely established. The exact mechanism of this

23. (*a*) Weir, J. F.: Association of Jaundice and Ascites in Diseases of Liver, J. A. M. A. **91**:1888 (Dec. 15) 1928. (*b*) Meyer, J., and Learner, A.: Ascites Occurring During Jaundice, with Recovery: Report of Case, ibid. **104**:114 (Jan. 12) 1935.

function is by no means completely understood. Under these circumstances one can only agree with the comment of Mann:[24]

> Although it is true that hepatic activity is an important factor in removing an excess of dextrose . . . the fate of dextrose in the animal organism depends on so many extrahepatic factors that only under very special conditions could a change in glucose tolerance indicate impaired hepatic function.

SUMMARY

1. The tolerance to dextrose (orally and intravenously administered), the icteric index and the bilirubin content of the blood were determined serially in 12 children with catarrhal jaundice.

2. The icteric index closely paralleled the serum bilirubin content of the blood.

3. Total cholesterol values were normal or below normal in all but 3 patients. The percentage of esters was decreased in 75 per cent of the children.

4. No correlation was found between the degree of icterus and the type of dextrose tolerance curve obtained.

5. Decreased tolerance to orally administered dextrose was frequently found when the response to the previous intravenous test had been normal.

6. When the intravenous test showed a decrease in tolerance the tolerance to orally administered dextrose was also decreased.

7. Improvement of a previously decreased tolerance to dextrose (orally or intravenously administered) usually accompanied clinical improvement and a decrease in the degree of icterus.

CONCLUSIONS

The dextrose tolerance (oral or intravenous) test is not a reliable procedure to indicate impaired hepatic function and is not a satisfactory aid in the differential diagnosis of jaundice.

Miss H. C. Lathrop and Mrs. E. L. Waldron gave technical assistance in the chemical determinations on the blood.

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24. Mann, F. C.: Hepatic Function in Relation to Hepatic Pathology, Ann. Int. Med. **8**:432, 1934.

RELATION OF DENTAL CARIES IN RURAL CHILDREN TO SEX, AGE AND ENVIRONMENT

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Marked differences of opinion exist regarding the etiology and practical control of dental caries. One group is apparently convinced that caries is entirely the result of oral environment. They believe that environment permits the growth of specific bacteria which produce acid, which in turn attacks the tooth structure. They discount the importance of metabolic influences from within the body. Their thesis is: Control or destroy this particular type of bacteria, or modify the conditions which favor bacterial invasion, and prevention and control of caries follow.

Others believe that improving the nutritional status of children alters the tooth itself so that it becomes caries resistant. On the other hand, when certain dietary defects occur the tooth loses its resistance.

Fundamentally, these two approaches are not incompatible. The one deals with bacterial invasion of a tissue, the other with resistance to such invasion. The distinction between these two functions in disease is well recognized in many fields of public health, and examples of measures of control based on protection against bacterial invasion, on the one hand, or on building up resistance, on the other, are fairly frequent. The practical problem, the prevention and control of dental caries, deals not so much with the more academic question of first or primary cause as with the relative values of measures based on one or the other of these two theses in reducing the incidence of tooth decay. Here the difference of opinion becomes very real.

Perhaps the sharpest point of disagreement in these diverse viewpoints concerns the role played by vitamin D. Numerous examples of this disagreement appear in the literature, but the following quotations will serve as illustrations:

> Children in the south who have plenty of vitamin D in the abundant sunshine have no rickets, but they have just as much dental disease as do those in the north where rickets is common.[1]

From the DeLamar Institute of Public Health, Columbia University College of Physicians and Surgeons.

1. Bunting, R.: The Prevention of Dental Caries, J. Michigan State Dent. Soc. **9**:66 (March) 1937.

We must remember that, in most countries, the problem of providing adequate dental treatment in schools for already existing caries is an insoluble one, and for this reason it behooves public health authorities to give closest attention to other possible methods of combating the disease.

. . . While encouraging the use of the toothbrush for social and aesthetic reasons, we may, at the same time, reflect that most of the sound teeth in the world are in the mouths of people who have never seen a toothbrush in their lives. Dental caries may be attacked by improving the diet of expectant and nursing mothers, infants and growing children, particularly in respect to its content of calcium, phosphorus and vitamin D.

It would be cheaper to supply schoolchildren regularly with vitamin D in some form than to supply them with dental treatment—treatment which, for the most part, consists in an attempt to repair the ravages of already existent caries. This is a question which merits the closest attention on the part of public health authorities.[2]

Since these recommendations were made by the Health Organization of the League of Nations other studies concerning vitamin D and dental caries have appeared. When children were fed graded amounts of vitamin D the response, measured as relative increase of carious tooth surfaces per child per hundred days as compared with the increase in untreated children serving as controls, was inversely proportionate to the amount of vitamin D fed.[3] A seasonable rhythm in the incidence of caries has been reported, the season most remote from the summer sun being associated with the greatest amount of new caries.[4] When children were exposed to artificially produced ultraviolet radiation under controlled conditions they had fewer cavities than did children who were not so exposed.[3] The two groups lived in the same institution and consumed the same food. The caries rates for groups of children have been found to be inversely proportionate to the amount of sunshine that prevails at their place of residence.[5] In all these studies, it seems reasonable to assume, the same physiologic process was involved. In the feeding experiments, the vitamin D was absorbed from the digestive tract. When the children's skins were exposed to the ultraviolet radiation, either artificial or solar, the vitamin D was formed in the skin and utilized by the body. Moreover, the response was apparently graded; that is, the larger amounts of vitamin D or sunlight were accompanied

2. Burnet, E., and Aykroyd, W. R.: Diet and the Teeth, in Nutrition and Public Health, Quart. Bull. Health Organ., League of Nations **4**:424, 1935.

3. McBeath, E. C., and Zucker, T. H.: The Role of Vitamin D in the Control of Dental Caries in Children, J. Nutrition **15**:547, 1938.

4. Erpf, S. F.: Dental Caries and Paradental Disturbances: II. The Seasonable Incidence of Dental Caries in Children, J. Am. Dent. A. **25**:681, 1938. McBeath and Zucker.[3]

5. East, B. R.: Mean Annual Hours of Sunshine and the Incidence of Dental Caries, Am. J. Pub. Health **29**:777, 1939.

by less caries. Artificial irradiation in addition to exposure to the sun likewise reduced the incidence of caries.

Total production of vitamin D in the body by exposure to ultraviolet radiation is dependent on the total amount of ultraviolet energy absorbed through the surface of the skin. The amount of energy is primarily dependent on the intensity of the rays reaching the surface of the skin and the length of exposure. It would seem to follow that children living in areas where climatic and other conditions are known to produce variations in the amount of solar ultraviolet radiation at the earth's surface or to modify the conditions of exposure should show corresponding differences in their mean caries rates.

This conclusion suggested a study which might produce convincing evidence in support of the present views concerning the protective value of vitamin D against dental caries. Such a study might also test the

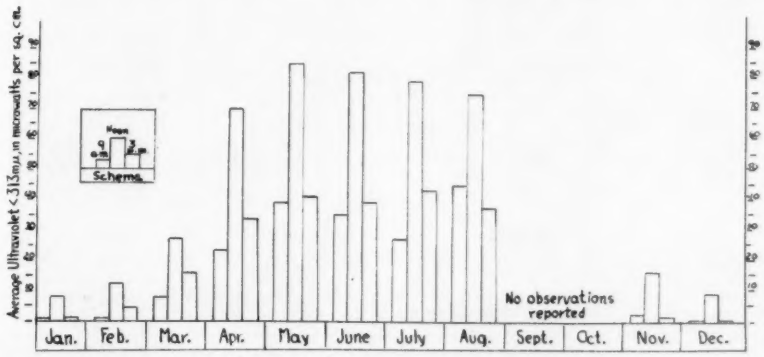

Chart 1.—Average monthly amount of ultraviolet radiation of less than 313 millimicrons wavelength at fifteen points in the United States (from data of Ives and Gill [6]).

validity of conclusions drawn from the feeding experiments and from observations on inhibition of caries formation by exposure to artificial ultraviolet radiation.

There are many conditions which can and do alter both the intensity of the ultraviolet radiation and the duration of exposure. Among these are: atmospheric pollution by dust, smoke and fog; temperature; wind velocity; clouds; number of hours of sunshine; humidity; latitude; altitude; ozone in the atmosphere; reflection from snow, clouds and surroundings, and "skyline." These conditions do not necessarily operate independently. They often overlap. For example, it has been shown that twice as much pollution of air exists in cities during the winter as in the summer. When the wind velocity is doubled there is a decrease of six tenths in the pollution of air. The amount of suspended material is also greater on cloudy than on clear days when

the temperature and the wind velocity remain the same. A decrease in vertical air currents on cloudy days is said to account for this difference.[6]

Snow reflects ultraviolet rays in an efficient manner. Where snow covers the ground during long periods of the year, reflection probably contributes appreciably to the total amount of radiant energy which reaches the skin.[7]

In this study we have employed the three climatic variables which gave the most promise of producing variation in the amounts of vitamin D from solar radiation in the skins of children: mean number of hours of sunshine per year, latitude and mean winter temperature.

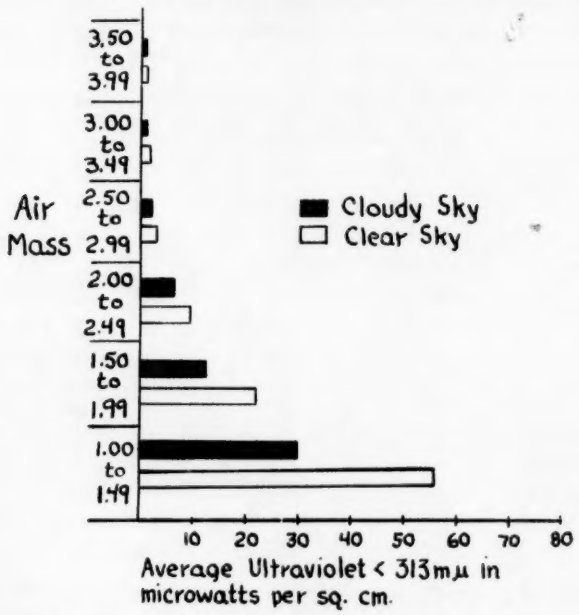
3.50 to 3.99
3.00 to 3.49
Air Mass 2.50 to 2.99
2.00 to 2.49
1.50 to 1.99
1.00 to 1.49
Cloudy Sky
Clear Sky
10 20 30 40 50 60 70 80
Average Ultraviolet < 313mμ in microwatts per sq. cm.

Chart 2.—Relation of amount of ultraviolet radiation to thickness of air mass.

We included mean annual hours of sunshine because that factor seemed the principal element in the duration of exposure. Except for slight differences, the sun is above the horizon about 51 per cent of the time, or about 4,450 hours, in all parts of the United States during the year. Thus the possible insolation for all localities of the United States is about the same. However, marked differences in the number of hours

6. Ives, J. E.; Britten, R. H.; Armstrong, D. W., and Goldman, F. H.: Atmospheric Pollution of American Cities for the Years 1931 to 1933, with Special Reference to the Solid Constituents of the Pollution, Public Health Bulletin 224, United States Treasury Department, Public Health Service, 1936.

7. Coblentz, W. W.; Stair, R., and Hogue, J. M.: Measurements of Ultraviolet Solar Radiation in Various Localities, J. Research **23**:133, 1933.

of sunshine at different localities in this area occur. Therefore, for purposes of this investigation a distinction is made between possible and actual hours of sunshine.

We have relied largely on the papers of Ives and Gill to support our hypothesis that differences in the number of hours of sunshine introduce measurable variations in the amount of available ultraviolet energy, although the literature contains other convincing evidence. They measured the ultraviolet solar radiation at fifteen points in the United States over a period of twenty-one months. We have summarized some of their data in table 1. There appears to be about twice as much effective ultraviolet radiation on clear as on cloudy days. This ratio is highest in the more northerly latitudes and is greatest at noon. We show the monthly values for the different hours of the day in chart 1.[8]

TABLE 1.—*Effect of Air Mass and Cloudiness on Amount of Solar Ultraviolet Radiation at Earth's Surface* *

Air Mass †	Average Amount of Ultraviolet Radiation of Wavelength < 313 μμ, Microwatts per Square Centimeter		Ratio
	Clear Sky	Cloudy Sky	
1.00 to 1.49	55.6	29.4	1.9
1.50 to 1.99	21.3	12.1	1.8
2.00 to 2.49	9.0	6.1	1.5
2.50 to 2.99	2.9	1.6	1.8
3.00 to 3.49	1.1	0.5	2.2
3.50 to 3.99	0.8	0.4	2.0

* Calculated from data on observations at fifteen points in the United States.

† Air mass, which is defined as the thickness of the layer of air through which the sun's rays must pass to reach the earth's surface, is approximately proportional to the cosecant of the sun's altitude and is measured in the same unit. Air mass when the sun is at the zenith altitude of 90 degrees is taken as unity.

Latitude was included for study because it appeared to be the single outstanding factor influencing variation in intensity of solar radiation. We have again freely used the work of Ives and Gill to support this thesis. The altitude of the sun at any hour of the day is a function of latitude. The air mass, or the thickness of the layer of air through which the sun's rays must pass to reach the earth's surface, is approximately proportional to the cosecant of the sun's altitude and is conveniently measured in the same unit. Thus, when the sun is at the zenith altitude of 90 degrees the air mass is taken as unity.

Ives and Gill measured the amount of ultraviolet energy as a function of the air mass for both cloudy and clear days. The measurements show a marked reduction in ultraviolet energy as the air mass increases, as indicated in table 1 and chart 2.

8. Ives, J. E., and Gill, W. A.: Measurements of Ultraviolet Radiation and Illumination in American Cities During the Years 1931 to 1933, Public Health Bulletin 233, United States Treasury Department, Public Health Service, 1937.

Our third variable, winter temperature, was selected because we considered it an additional factor in the duration of exposure to as well as in the intensity of solar radiation. Different winter temperatures might cause children to remain indoors out of the available sunshine to varying extents. The different types of winter clothing required by differing temperatures might affect the degree of interference with the intensity of the ultraviolet rays at the skin's surface or the amount of exposure of the skin. It was thought that in the temperate zone temperatures at other seasons would not differ enough to influence materially either the length of time spent out of doors or the amount and type of clothing worn.

To test the possible relation between incidence of caries and these three environmental factors, we have selected the caries rates for children residing in 358 rural or semirural counties of twenty-four states of the United States. There were a total of 581,708 children in the groups

TABLE 2.—*Mean Caries Rates in Permanent Teeth per Hundred Children in 358 Counties of the United States*

	Sex					
	Boys			Girls		
Age, Years	6-8	9-11	12-14	6-8	9-11	12-14
Mean	97.3	218.0	348.5	110.0	240.0	384.0
σ mean	2.6	4.7	7.3	2.9	5.0	7.7

studied, about equally divided according to sex. They were classified in groups according to age, namely, 6 to 8, 9 to 11 and 12 to 14 years. Only white children were included, and only caries in permanent teeth was considered in the present study.

The 358 counties for which the caries rates were determined are geographically distributed in about the same way as the locations for the measurements of ultraviolet energy of Ives and Gill.

Rural children were selected for study because it was thought that they would be ethnologically more uniform than city children. It was also thought that the food of rural children would introduce fewer variables than that of city residents, that the amount of dust and smoke in the air would be less and more uniform [9] and that housing and living conditions would be less variable. Only white children were studied to exclude as far as possible the variable which cutaneous pigmentation might introduce.

The data on which the caries rates are based were collected under the direction of the American Dental Association and the United States

9. These examinations were made during 1933-1934. The ages of the children preclude the possibility of their being greatly affected by the recent dust storms.

Public Health Service [10] and were published by the Public Health Service. We have described the method of calculating the rates elsewhere.[5] To make the groups as homogeneous as possible, frequency distribution tables were arranged according to age and sex. The mean caries rates for the various age-sex groups are shown in table 2.[11]

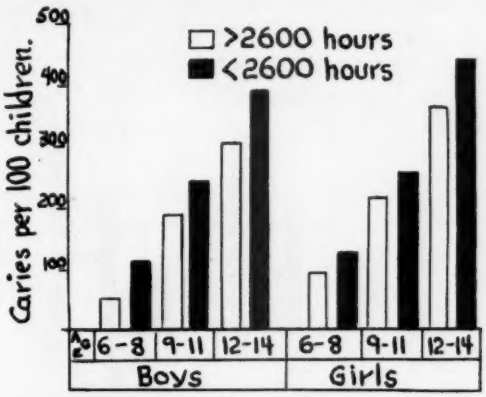

Chart 3.—Relation of mean caries rate for permanent teeth of children of twelve age-sex groups to number of hours of sunshine.

TABLE 3.—*Relation of Mean Caries Rate for Permanent Teeth per Hundred Children and Mean Number of Hours of Sunshine per Year*

	Boys					
	Age, Years					
	6-8		9-11		12-14	
Mean number of hours of sunshine *	>2,600	<2,600	>2,600	<2,600	>2,600	<2,600
Mean caries rate per 100 children	64.5	114.0	195.5	245.0	305.7	303.5
σm	4.6	4.1	5.9	7.3	8.7	10.8
D ($m_1 - m_2$)	48.0 ± 6.1		49.5 ± 9.4		87.8 ± 13.6	
X/σ	7.8		5.2		6.4	
	Girls					
	Age, Years					
	6-8		9-11		12-14	
Mean number of hours of sunshine *	>2,600	<2,600	>2,600	<2,600	>2,600	<2,600
Mean caries rate per 100 children	97.5	125.5	215.0	268.0	340.0	440.0
σm	3.3	4.6	6.1	6.8	9.5	11.7
D ($m_1 - m_2$)	28.0 ± 5.6		53 ± 9.1		100 ± 15	
X/σ	5.0		5.8		6.6	

* In 190 counties the mean number of hours of sunshine was greater and in 168 it was less than 2,600 per year.

10. Messner, C. T.; Gafafer, W. M.; Cady, F. C., and Dean, H. T.: Dental Survey of School Children, Ages Six to Fourteen Years, Made in 1933-1934 in Twenty-Six States, Public Health Bulletin 226, United States Treasury Department, Public Health Service, 1936.

11. The frequency distribution tables appeared in a previous paper.[5]

Evidence regarding the suitability of the data for purposes of comparing the caries rate of one county with that of another has been previously presented.[12]

The frequency distribution of caries rates of 358 counties of twenty-four states based on white boys and girls of three age groups residing in rural and semirural areas closely follow the normal law of distribution except as influenced by variables

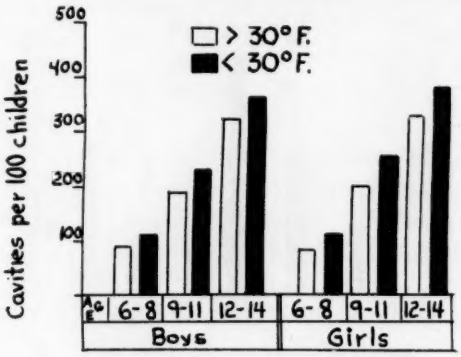

Chart 4.—Relation of mean caries rate to mean winter temperature.

TABLE 4.—*Relation of Mean Caries Rate for Permanent Teeth per Hundred Children and Mean Winter Temperature*

	Boys					
	Age, Years					
	6-8		9-11		12-14	
Mean winter (F.) temperature *	>30	<30	>30	<30	>30	<30
Mean caries rate per 100 children	91.0	111.5	189.5	229.8	326.0	362.0
σ m	8.8	6.2	8.0	5.2	6.4	4.3
D ($m_1 - m_2$)	20.5 ± 10.7		40.3 ± 11.0		36.0 ± 7.7	
X/σ	1.9		3.7		4.7	
	Girls					
	Age, Years					
	6-8		9-11		12-14	
Mean winter (F.) temperature *	>30	<30	>30	<30	>30	<30
Mean caries rate per 100 children	84.0	118.5	208.0	258.0	340.7	384.5
σ m	9.5	6.8	8.5	5.7	6.7	5.9
D ($m_1 - m_2$)	34.5 ± 11.7		50.0 ± 10.4		43.8 ± 8.9	
X/σ	2.9		4.8		4.9	

* In 134 counties the mean winter temperature was higher than 30 F., and in 224 counties it was lower.

which in themselves are likewise distributed according to the same law. The data appear, therefore, to be suitable for comparing the caries rates of one group with another. They also seem adequate as the basis for determining the correlation of caries rates with other variables.

12. East, B. R., and Kaiser, H.: Association of Dental Caries in Children with Sex, Age and Environment, J. Am. Dent. A. **27**:1430 (Sept.) 1940.

The data on which the mean number of annual hours of sunshine in the various counties are based were collected and published by the United States Weather Bureau.[18]

There were 190 counties having more and 168 having less than 2,600 hours of sunshine per year. The groups living where the most sunshine prevails had in every instance the lowest caries rates. The differences between the mean caries rates for comparable age-sex groups when compared with their standard errors are of a magnitude to make their significance from a statistical standpoint highly probable. The rates and their standard errors are shown in table 3 and chart 3.

The data for the mean winter temperatures are also from the records of the United States Weather Bureau. There were 134 counties in our series with a mean winter temperature higher and 224 with a mean winter temperature less than 30 F. The groups who resided in zones where the mean temperature was below 30 F. had higher caries rates than those who lived where the mean temperature was higher. The differences between the mean caries rates for the comparable age-sex groups in areas with low temperatures and those in the localities with higher temperatures were so much larger than the standard errors of their differences that the values appear significant. The values are given in table 4 and chart 4.

In our study, 169 counties were north and 189 were south of latitude 40 north. In every instance the children living in the northern zone had the higher mean caries rate. The ratios of the standard errors to the differences are such as to establish their statistical significance. The values are given in table 5 and chart 5.

To determine the degree of relation between the caries rates and the three environmental factors, the correlation coefficients of the eighteen possible combinations were computed. In these determinations all the class intervals of the environmental factors given in table 6 were used. The results are summarized in table 7. The greatest value in the series is 0.55. In most problems correlation coefficients of this magnitude would be considered of little importance. In this case, however, they are extremely suggestive. First, they are statistically significant, as evidenced not only by their standard error but also by the general homogeneity of the set. Second, they are admittedly only partial correlations. As such, to the extent that each variable contributes to the determination of the caries value it necessarily detracts from the contri-

13. Weather Map 13, United States Department of Agriculture, Weather Bureau, 1936. Atlas of American Agriculture, United States Department of Agriculture, Weather Bureau, 1936.

bution of the other two. High coefficients in all three variables would be impossible, since two of these variables are themselves closely correlated.

We have called attention to the fact that latitude and number of hours of sunshine overlap in affecting the mean amount of ultraviolet energy available from solar radiation at any given locality.[14] Mean

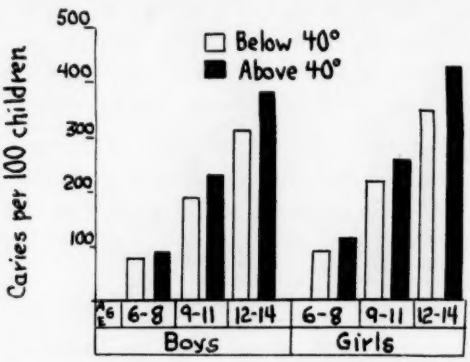

Chart 5.—Relation of mean caries rate to latitude.

TABLE 5.—*Relation of Mean Caries Rate for Permanent Teeth per Hundred Children and Latitude of Residence*

	Boys					
	Age, Years					
	6-8		9-11		12-14	
Latitude *	>41°	<41°	>41°	<41°	>41°	<41°
Mean caries rate per 100 children	83.7	99.0	197.5	233.0	312.0	385.0
σ m	3.9	3.5	6.7	5.8	10.4	9.3
D ($m_1 - m_2$)	15.3 ± 5.2		35.5 ± 8.9		73.0 ± 14.0	
X/σ	2.9		4.0		5.2	
	Girls					
	Age, Years					
	6-8		9-11		12-14	
Latitude *	>41°	<41°	>41°	<41°	>41°	<41°
Mean caries rate per 100 children	98.5	114.2	220.0	260.5	349.0	429.0
σ m	3.8	3.6	7.2	6.2	11.3	10.0
D ($M_1 - m_2$)	15.7 ± 5.2		40.5 ± 9.5		80.5 ± 15.0	
X/σ	3.0		4.2		5.3	

* One hundred and eighty-nine counties were south and 169 were north of latitude 41 north.

winter temperature, hours of sunshine and latitude are likewise variables in their relation to one another. For example, southern Louisiana and

14. It is recognized that diurnal variations in air mass occur. It has been assumed that differences in time of day when the sun would be recorded as "shining" would tend to be equalized over such a period of years as is represented by the ages of the children in this study.

northern Minnesota have the same number of hours of sunshine but differ greatly in mean winter temperature and latitude. Northern Maine and northwestern Washington have approximately the same amount of sunshine and the same latitude but differ greatly in mean winter tem-

TABLE 6.—*Class Intervals of Environmental Factors*

Sunshine (Mean Number of Yearly Hours)	Temperature (Mean Winter), F.	Latitude
Less than 2,200	0 to 10	Below 37° 50′
From 2,200 to 2,599	10 to 20	37° 50′ to 42° 50′
From 2,600 to 2,999	20 to 30	Above 42° 50′
More than 3,000	30 to 40	
	40 to 50	
	50 to 60	

TABLE 7.—*Correlation Coefficients for Caries Rate for Permanent Teeth per Hundred Children and Mean Number of Annual Hours of Sunshine, Mean Winter Temperature and Latitude in 358 Rural Counties of the United States*

	Boys								
	Climatic Variant								
	Sunshine			Winter Temperature			Latitude		
Age, years	6-8	9-11	12-14	6-8	9-11	12-14	6-8	9-11	12-14
r	−0.42	−0.21	−0.39	−0.10	−0.28	−0.28	0.17	0.37	0.40
σ		0.05			0.05			0.05	
	Girls								
	Climatic Variant								
	Sunshine			Winter Temperature			Latitude		
Age, years	6-8	9-11	12-14	6-8	9-11	12-14	6-8	9-11	12-14
r	−0.38	−0.26	−0.27	−0.19	−0.29	−0.38	0.14	0.38	0.55
σ		0.05			0.05			0.05	

TABLE 8.—*Correlation Coefficients for Mean Number of Annual Hours of Sunshine, Mean Winter Temperature and Latitude in 358 Counties of the United States*

	Environmental Combination		
	Sunshine and Latitude	Sunshine and Winter Temperature	Latitude and Winter Temperature
r	−0.038	+0.024	−0.96
σ	0.05	0.05	0.05

perature. The correlation coefficients of three possible combinations of environmental variants are shown in table 8.

As it appeared that varying degrees of relation exist between the independent variables and the groups with different caries rates, as well as between the independent variables themselves, in the 358 localities from which our samples were drawn, a formula was required which,

"taking account of all three variates at each station, and agreeing as near as possible with the values recorded," [15] would measure the relation of the caries rate and each of the independent variables in our series, free from the influence of the remaining two. Such a formula is the partial regression equation described by Fisher.[15]

In our case this partial regression equation has the form: $c = C - S(s - 2{,}600) - T(t - 25.5) + L(l - 40.6)$, in which c = the mean caries rate for permanent teeth in an age-sex group in any county, C, the mean rate for the same age-sex group in 358 counties, s, t and l, hours of sunshine, mean winter temperature and latitude of the county,

TABLE 9.—*Partial Regression Coefficients for the Mean Caries Rates for Permanent Teeth per Hundred Children and the Mean Number of Annual Hours of Sunshine, Mean Winter Temperature and Latitude in 358 Counties in the United States*

	Boys								
	Climatic Variant								
	Add 100 Hours of Sunshine per Year			Add 10 F. to Mean Winter Temperature			Add 1° to Latitude		
Age, years.....	6-8	9-11	12-14	6-8	9-11	12-14	6-8	9-11	12-14
Partial regression coefficient..	—7.25	—8.6	—18.0	—3.5	—6.0	—21.0	2.6	8.9	18.0
σ	0.99	1.75	2.5	4.25	8.0	12.0	1.3	2.3	3.2
X/σ	7.3	4.9	7.2	0.8	0.7	1.7	2.0	3.8	5.6
	Girls								
	Climatic Variant								
	Add 100 Hours of Sunshine per Year			Add 10 F. to Mean Winter Temperature			Add 1° to Latitude		
Age, years.....	6-8	9-11	12-14	6-8	9-11	12-14	6-8	9-11	12-14
Partial regression coefficient..	—6.9	—11.5	—21.0	—11.8	—7.5	—65.0	1.2	10.0	23.4
σ	1.7	2.5	2.5	4.8	8.0	11.0	1.3	2.2	3.0
X/σ	4.0	4.6	8.4	2.5	0.9	5.5	0.9	4.5	7.8

and S, T and L, the corresponding regression coefficients computed to yield the best mathematical fit to all the data. Stated in nonmathematical terms, the partial regression equation sets up the following relation in quanitative form.

In each county the mean caries rate for the permanent teeth of a specified age-sex group is made up of: (1) the mean rate of that group in the 358 counties, (2) minus the regression coefficient of the hours of sunshine times the excess of hours of sunshine of that county over 2,600 hours (or plus the regression coefficient of the hours of sunshine times the number of hours of sunshine under 2,600), (3) minus the regression coefficient of the mean winter temperature times the excess in mean

15. Fisher, R. A.: Statistical Methods for Research Workers, London, Oliver & Boyd, 1936.

winter temperature over 25.5 F. (or plus the regression coefficient of the mean winter temperature times the deficiency below 25.5 F.), (4) plus the regression coefficient of the latitude of the county times the value for the latitude of the county above 40.6 degrees (or minus the regression coefficient of the latitude of the county times the value for the latitude under 40.6 degrees).

In table 9 appear the partial regression coefficients of the caries rates for the permanent teeth of the various age-sex groups and the environmental factors. These coefficients are given for the influences on the caries rates for the permanent teeth of the addition of 100 hours of sunshine, 10 degrees (F.) of winter temperature or 1 degree of latitude

TABLE 10.—*Effect on Mean Caries Rate for Permanent Teeth per Hundred Children in 358 Counties of Changes in Number of Annual Hours of Sunshine, Mean Winter Temperature and Latitude*

	Boys								
	Climatic Variant								
	Add 100 Hours of Sunshine per Year			Add 10 F. to Mean Winter Temperature			Add 1° to Latitude		
Age, years.....	6-8	9-11	12-14	6-8	9-11	12-14	6-8	9-11	12-14
Percentage change from mean caries rate.....	—7.4	—3.9	—5.2	—3.6	—2.7	—6.0	2.7	4.1	5.2
σ	1.0	0.8	0.7	4.5	3.8	3.5	1.3	1.1	0.9
X/σ	7.3	4.9	7.2	0.8	0.7	1.7	2.0	3.8	5.6
	Girls								
	Climatic Variant								
	Add 100 Hours of Sunshine per Year			Add 10 F. to Mean Winter Temperature			Add 1° to Latitude		
Age, years.....	6-8	9-11	12-14	6-8	9-11	12-14	6-8	9-11	12-14
Percentage change from mean caries rate.....	—6.3	—4.7	—5.5	—10.7	—3.2	—16.7	1.1	4.2	6.1
σ	1.6	1.0	0.6	4.3	3.3	2.8	1.2	0.9	0.8
X/σ	4.0	4.6	8.4	2.5	0.9	5.9	0.9	4.5	7.8

to the mean annual amounts of these factors prevailing at the places of residence of the group of children of the particular age and sex.

In table 10 we give the percentage from the mean rates for the various age-sex groups associated with the various independent variables. These percentage values have been computed from the partial regression coefficients, the class intervals of the independent variables shown in table 6 and those of the original frequency distribution tables for caries being taken into account. In chart 6 these percentage relationships are shown graphically.

The relation of caries rate to latitude and sunshine is what might be expected from the measures of ultraviolet solar radiation if vitamin D is an etiologic factor in caries. The greater the amount of sunshine

available at a given location, the lower is the caries rate. The more northerly a county, the higher is the caries rate of the children. The values are all consistently in agreement with our hypothesis.

The lowest values in the sunshine series indicate that each additional 100 hours of sunshine is associated with a decrease of 3.92 ± 0.8 and 4.7 ± 1.0 per cent from the mean rates of caries in the permanent teeth of boys and girls, respectively, in the 9 to 11 year groups. The highest values are in the 6 to 8 year groups, which show respective decreases of 7.4 ± 1.0 and 6.3 ± 1.6. The values for the 12 to 14 year groups are intermediate.

In our latitude series we find that with each increase of 1 degree of latitude there is a percentage increase of 2.7 ± 1.3 in the caries rates for boys of 6 to 8 years. For girls of the same age the increase of the

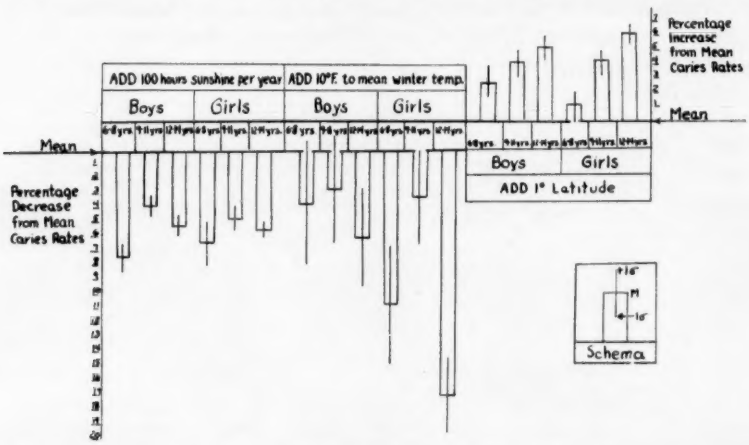

Chart 6.—Effect on mean caries rate for permanent teeth of changes in number of hours of sunshine per year, in mean winter temperature and in latitude in twelve age-sex groups of children residing in 358 rural counties of the United States.

mean rate is 1.1 ± 1.2 per cent. The other age groups show important and statistically significant percentage increases. The lowest value for the groups of 9 to 11 and 12 to 14 years is 4.1 ± 1.1 per cent for each degree of latitude.

When the overlapping influences of sunshine and latitude are separated out, there is little relation of winter temperature to caries rates, except for the girls in the age groups of from 6 to 8 and 12 to 14 years. For all the boys and for the girls in the age groups from 9 to 11, the standard errors are of such a magnitude in relation to the percentage change as to make it appear that winter temperatures exert little effect on the caries rates. However, the indicated change in all four groups is in the same direction, the direction anticipated from the effect of lower temperature on body exposure.

In the oldest and youngest groups of girls winter temperature apparently played an important role in incidence of caries. Why is there this difference? We offer the following speculations: Is it possible that the youngest girls are kept indoors out of the available sunshine in the cold weather, while boys of the same age are not? Are girls from 9 to 11 years old tomboyish, and do they go out of doors in the winter time in the same manner as apparently do boys of all ages? And do the girls of 12 to 14 years of age remain indoors when it is cold? Perhaps the rural girls aged 12 to 14 have indoor duties, while boys of the same age find both their recreation and their tasks outside in what available sunshine there is.

From the values in table 9 the mean caries rates for children of age-sex groups corresponding to our groups, residing in rural or semirural areas of the United States with a known mean annual amount of sunshine expressed in hours, mean annual winter temperature and latitude can be estimated from the partial regression equation.

SUMMARY

We have determined by the partial regression equation the partial regression coefficients of the relation of dental caries and three climatic factors—mean annual hours of sunshine, mean winter temperature and latitude—prevailing in 358 rural or semirural counties.

By these methods it appears that an important relation exists between the incidence of caries and the amount of sunshine and latitude.

Winter temperature is apparently of only slight importance in the incidence of caries in all boys and in girls aged 9 to 11 years. In girls aged 6 to 8 and 12 to 14 this climatic factor has an important correlation with the incidence of dental caries.

These results are in agreement with the conditions which are known to affect the amount of solar ultraviolet radiation.

The results of this study are in agreement with those obtained by feeding children vitamin D under controlled conditions and also with the observations made on inhibition of caries by exposing children's skins to artificially produced ultraviolet light.

The reports of seasonable rhythm in the occurrence of caries are now more easily understandable.

Our results support the soundness of the recommendation by the Health Organization of the League of Nations that public health authorities should give "closest attention" to the role vitamin D could play in the prevention and control of dental caries.

RESULTS OF SCHICK TEST IN CHILDREN ONE TO TEN YEARS AFTER INJECTIONS OF TOXOID

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In a previous survey of children who were given injections of diphtheria toxoid in the health centers of the Child Welfare Association of Montreal from 1926 to the end of 1934, it was found that there was a larger proportion of positive Schick reactions as the interval between the last dose of toxoid and the Schick test was prolonged.[1] A further study was carried out to determine whether there was a progressive loss of immunity as the years following the administration of toxoid increased, as well as to determine the number of children whose reactions, after having previously been negative, reverted to positive.

Children who had received injections of diphtheria toxoid from one to ten years before and who were available were given Schick tests. Some who were inoculated earlier had two doses; all the others had three doses. No Schick tests were done on any of the children prior to inoculation. Eight hundred and fifty-three had had Schick tests performed on them six months or more after the last dose of diphtheria toxoid, so that they were now subjected to a second test; 35 had had two previous tests, while for the remainder this was the first test. Children who had received less than two injections of toxoid, as well as any who had been given injections of diphtheria antitoxin, were not included.

SCHICK TESTS

All the Schick tests were read on the fifth day after they were done. They were all performed on the anterior surface of the forearm by the intradermal injection of 0.1 cc. of a dilution of diphtheria toxin which

From the Child Welfare Association of Montreal; the Departments of Paediatrics and of Public Health and Preventive Medicine, McGill University, and the Department of Epidemiology and Biometrics, School of Hygiene, University of Toronto.

1. Benjamin, B.; Fleming, G., and Ross, M. A.: Results of Schick Test in 5,195 Children Given Injections of Diphtheria Toxoid, Am. J. Dis. Child. **55**:51 (Jan.) 1938.

conforms to the League of Nations' standard requirements for combining power and toxicity,[2] and a similar control injection of 0.1 cc. of approximately a 1 : 100 dilution of toxoid was made on the anterior surface of the other forearm of every child. The material used was prepared and properly tested as to potency by the Connaught Laboratories, University of Toronto.

In a previous communication [1] we have discussed certain reservations which must be made in judging immunity by the Schick test. Although it is unquestionably inadequate as an exact measure of immunity, its practical value in the determination of susceptibility to the development of clinical diphtheria in most cases is definitely established. Proved diphtheria has been known to develop in persons with negative reactions to the Schick test, but this is a comparatively rare occurrence.[3]

Therefore the level of immunity as gaged by the Schick test is of considerable value as a dividing line between those persons in whom the disease might presumably develop under conditions of close contact with the diphtheria bacillus and those in whom in all probability it would not, accordingly as they reacted positively or negatively to the test.

TABLE 1.—*Data Concerning 1,522 Children Given Schick Tests*

Schick Test	2 Doses	3 Doses
One test	39	517
Second test without further toxoid	78	853
Second test after 1 more dose of toxoid	8	27
Total	125	1,397

RESULTS

Table 1 shows that the group consisted of 1,522 children. Thirty-nine had had only two doses of toxoid and no previous Schick test; 78 had had two doses of toxoid and a previous Schick test; 517 had had three doses of toxoid and no previous Schick test; 853 had had three doses of toxoid as well as a previous Schick test; 8 had a second test after the third dose of toxoid, and 27 had a second test after a fourth dose of toxoid.

2. Fraser, D. T., in Report of the Permanent Commission on Biological Standardisation (London), Series III, League of Nations Publications, no. C. H. 1056 (I), Boston, World Peace Foundation, 1931.

3. O'Brien, R. A.; Okell, C. C., and Parish, H. J.: "Diphtheria" in Schick-Negative Reactors, Lancet **1**:149 (Jan. 19) 1929. Dudley, S. F.; May, P. M., and O'Flynn, J. A.: Active Immunization Against Diphtheria, Medical Research Council, Special Report Series, no. 195, London, His Majesty's Stationery Office, 1934. Benjamin, Fleming and Ross.[1]

The distribution of the children by age and sex reveals that the totals for the two sexes were almost equal and that there was the usual slightly greater number of boys in the first year of life.

Table 2 reveals that 22, or 18.4 per cent, of the group given two doses and 96, or 7.0 per cent, of the group given three doses had positive reactions. The reactions of 1 child in the former group and of 4 children in the latter were doubtful; they are excluded from the table. For the group given two doses the figures are too small to allow of any comparison; however, they support the conclusion, previously reported,[1] that

TABLE 2.—*Results of Present Schick Tests Excluding Reactions Which Were Doubtful or Not Read* *

Schick Test	2 Doses	3 Doses
Total tested	120	1,370
Number negative	98	1,274
Number positive	22	96
Percentage positive	18.4	7.0

* One reaction in the group given two doses of toxoid and 4 in the group given three doses were doubtful.
Four reactions in the group given two doses and 23 in the group given three doses were not read.

TABLE 3.—*Results of Present Schick Tests in Children who Received Three Doses of Toxoid* *

Interval in Years After Third Dose	Negative	Positive	Total	Percentage Positive
Less than 1	9	0	9	0
1- 2	197	10	207	4.8
2- 3	352	10	362	2.8
3- 4	261	12	273	4.4
4- 5	147	12	159	7.5
5-11	285	50	335	14.9
Total	1,251	94	1,345	7.0

* Excluding reactions which were doubtful or not read.

a lesser degree of immunity, as gaged by the Schick test, is induced by two doses than by three doses of toxoid.

As the data for the group given two doses are too limited to be of significance, they will be disregarded, and only those relating to the group given three doses will be analyzed in the remaining tables.

In table 3 are recorded the percentages of positive reactions obtained at yearly intervals after the third dose of toxoid in the group given three doses. A marked increase is noted after five years. A positive reaction was elicited in 14.9 per cent of the children after a period varying from five to eleven years. This is twice the percentage of positive reactions noted in the period from four to five years after the third dose of toxoid.

Table 4 gives the percentages of positive reactions obtained at yearly intervals after the third dose of toxoid among the children who had had a previous Schick test as compared with those who had not. Of 832 who had had a previous Schick test, 712 were tested in less than one year, 58 in from one to two years, 59 in two years and over after the third dose of toxoid; in 3 instances the interval was not stated. Up to the end of the fifth year, the advantage seems to be with those who had a

TABLE 4.—*Results of Present Schick Tests in Groups With and Without Previous Schick Test* *

Interval in Years After Third Dose	With Previous Schick Test				Without Previous Schick Test			
	Negative	Positive	Total	Percentage Positive	Negative	Positive	Total	Percentage Positive
Less than 1.....	..	..	..	...	9	0	9	0
1- 2	61	0	61	0	136	10	146	6.8
2- 3	186	6	192	3.1	166	4	170	2.4
3- 4	182	7	189	3.7	79	5	84	6.0
4- 5	110	8	118	6.8	37	4	41	9.8
5- 6	87	18	105	17.1	25	0	25	0
6- 7	70	18	88	20.4	20	0	20	0
7- 8	53	9	62	14.5	10	0	10	0
8- 9	10	2	12	16.7	5	2	7	28.6
9-10	3	1	4	25.0	1	0	1	0
10-11	1	0	1	0	..	..	..	...
Total.....	763	69	832	8.3	488	25	513	4.9

* Excluding those children who received extra toxoid.

TABLE 5.—*Results of Two Schick Tests in Children Who Received Three Doses* *

First Schick Test	Number †	Second Schick Test		
		Negative	Positive	Percentage Positive
Negative.....	799	732	67	8.4
Positive.....	13	13	0	0
Not read.....	20	18	2	10.0
Total.....	832	763	69	8.2

* Second test was performed without giving additional toxoid after first test.
† Data for 21 children whose second tests were not read are not included.

previous test. For the later years, the advantage is not maintained and would appear to be in favor of those who did not have a previous test. One would hardly suggest that a previous Schick test would increase the number of positive reactors, although it is possible that the stimulus of the test may wear off after about five years. The figures in the group without a previous test become so small in the later years that it is hard to draw any conclusions. The difference in the totals for the two groups is undoubtedly due to their different distribution.

The results of two Schick tests without further toxoid in the interval between the tests are shown in table 5. Of 799 children who reacted negatively to the first test, 67, or 8.4 per cent, reacted positively to the

second. Thirteen children who showed positive reactions to the first test reacted negatively to the second. This may have been due to a variation inherent in the test, but the stimulus provided by the toxin and toxoid injected when the first test was done [4] and possible latent immunization from subclinical infection with diphtheria bacilli may have been contributing factors.

An analysis of the reaction to the present Schick test according to the result of the previous test and the interval after the third dose (with no further toxoid given) shows that the reactions of none of the children reverted from negative to positive in less than two years. Of the 67 children who gave negative reactions to the first test and reacted positively on the second test, which took place after a period varying from two to ten years, the reactions of 5 became positive in from two to three

TABLE 6.—*Results of Present Schick Tests According to Age at First Dose*

Age in Months	Negative	Positive	Total	Percentage Positive
Under 6	32	1	33	3.0
6	80	5	85	5.9
7	84	3	87	4.6
8	94	2	96	2.1
9	79	3	82	3.6
10	61	7	68	10.3
11	69	10	79	12.6
12	72	3	75	4.0
Over 1 year.....	662	60	722	8.3
Not stated.....	18	..	18	...
Total.....	1,251	94	1,345	7.0

years, of 6 in from three to four years, of 8 in from four to five years and of 48 in from five to ten years.

Twenty-seven children, of whom 19 had positive and 8 doubtful reactions on the first test, were given an additional 1 cc. of toxoid. The reactions of 23 of these became negative, those of 2 remained positive and the tests of 2 were not read.

In table 6 the percentages of positive reactions to the present Schick test have been listed according to the various ages at which the children received their first dose of toxoid. The figures are small. However, there is no appreciable difference between those who were inoculated at the ages of 6, 7 and 8 months and those who were older.

Table 7 shows that the percentages of children whose reactions reverted from negative, after three injections of toxoid, to positive were not greater in the groups of children who were 6, 7 and 8 months old when they received their first dose than in the groups of those who were older.

4. Fraser, D. T., and Halpern, K. C.: Serial Titrations of Diphtheria Antitoxin Following Toxoid, Canad. Pub. Health J. **26**:476 (Oct.) 1935.

TABLE 7.—*Results of Two Schick Tests According to Age at Receiving First Dose*

Result of Present Test	Result of Previous Test: Negative — Age in Months at First Dose											Result of Previous Test: Positive — Age in Months at First Dose			Not Read
	1-5	6	7	8	9	10	11	12	Over 1 Yr.	Not Stated	Total	10	Over 1 Yr.	Total	Total
Negative (763)	12	43	36	46	42	33	44	56	414	6	732	1	12	13	18
Positive (69)	1	2	1	2	..	3	5	3	50	..	67	..	..	..	2
Percentages Positive (8.29)	7.6	4.4	2.7	4.1	..	8.3	10.2	5.0	10.7	..	8.3	..	..	..	10.0
Total.....	13	45	37	48	42	36	49	59	464	6	799	1	12	13	20

More of the younger infants would probably have reacted negatively to the Schick test prior to inoculation owing to passive immunity derived from the mother, but this would have been lost after the long intervals between administration of toxoid and Schick tests. Therefore, judging by and within the limits of the test, one may expect as good immunization when injections of toxoid are begun at 6 months of age as later.

This observation does not support the view [5] that infants under 1 year old are not as readily immunized as older ones. Diphtheria is encountered in infants before the age of 1 year. Moreover, several months may elapse after inoculation with toxoid is started before the infant acquires sufficient immunity to give a negative Schick reaction.

TABLE 8.—*Results of Present Schick Tests According to Sex in Children Given Three Doses* *

Interval in Years After Third Dose	Boys				Girls			
	Negative	Positive	Total	Percentage Positive	Negative	Positive	Total	Percentage Positive
Less than 1.....	4	0	4	0	5	0	5	0
1- 2	89	4	93	4.3	108	6	114	5.2
2- 3	166	5	171	2.9	186	5	191	2.6
3- 4	137	5	142	3.5	124	7	131	5.4
4- 5	74	4	78	5.1	73	8	81	9.9
5- 6	55	9	64	14.1	57	9	66	13.6
6- 7	48	10	58	17.2	42	8	50	16.0
7-11	52	6	58	10.4	31	8	39	20.4
Total.....	625	43	668	6.4	626	51	677	7.5

* Excluding reactions which were doubtful or not read.

It would appear therefore that the age recommended for immunization by some authors,[6] particularly Ramon [7] who has advised inoculation after 1 year of age, may be safely and advantageously placed earlier.

Table 8 gives the percentages of children who reacted positively to the present Schick test according to sex and interval after the third dose of toxoid. There is no appreciable difference in the totals for the two sexes, and the subtotals support the observation made in table 3 that there is an abrupt increase in the percentages of positive reactions after

5. Ramon, G., and Debré, R.: Persistence et valeur de l'immunité antitoxique chez les sujets vaccinés au moyen de l'anatoxine diphtérique, Presse méd. **38**:841 (June 21) 1930.

6. Greengard, J., and Bernstein, H.: Passive Immunity in Infants and Their Response to Diphtheria Toxoid: Preliminary Report, J. A. M. A. **105**:341 (Aug. 3) 1935. Blum, J.: Age Factor in Active Immunization of Infants Against Diphtheria, ibid. **98**:1627 (May 7) 1932.

7. Ramon, G.: La vaccination au moyen de l'anatoxine diphtérique et la prophylaxie de la diphtérie, Presse méd. **46**:1049 (July 2) 1938.

the fifth year. This is all the more significant in view of the well established decrease in the number of positive reactors to the Schick test in groups of older children who have received no inoculation against diphtheria as compared with younger ones.[8]

On the basis of these observations, it would seem desirable to take account of the status of immunity in the sixth year of life of all children who have been inoculated in infancy, in order to insure the presence of an adequate amount of circulating antitoxin in their blood. This could be accomplished by performing a Schick test at this time and if a positive reaction is elicited injecting 1 cc. of toxoid subcutaneously. A simpler and more economic procedure in a public health program would be to administer 1 cc. of toxoid to all children at this age. This procedure would also raise the level of immunity of those children who may have lost antitoxin to the point where they possess just enough to give a negative reaction to the test but whose reaction would very likely soon revert

TABLE 9.—*Results of First Schick Test According to Total Amount of Toxoid* *

Amount of Toxoid (3 Doses), Cc.	Negative	Positive	Total	Percentage Positive
1.5	11	..	11	...
2	608	33	731	4.5
2.5	548	21	569	3.7
3	22	..	22	...
Not stated.....	29	3	32	9.4
Total.....	1,308	57	1,365	4.2

* Excluding reactions which were doubtful or not read.

to positive. Severe local or general reactions at this age are rare.[9] Of course, in the case of a child giving a history of unusual reaction following previous injection of toxoid, a smaller dose, for example, 0.5 or even 0.1 cc., may be administered. Ramon [7] and Fraser [10] found a similar loss of immunity in children after immunization with diphtheria toxoid and also recommended reenforcement of immunity by a subsequent "recall" or reenforcing dose.

8. von Gröer, F., and Kassowitz, K.: Studien über die normale Diphtherieimmunität des Menschen, Ztschr. f. Immunitätsforsch. u. exper. Therap. **23**: 108, 1914. Park, W. H., and Zingher, A.: Diphtheria Immunity: Natural, Active and Passive; Its Determination by the Schick Test, Am. J. Pub. Health **6**:431 (May) 1916.

9. Fitzgerald, J. G.: Diphtheria Toxoid as an Immunizing Agent, Canad. M. A. J. **17**:524 (May) 1927. Moloney, P. J.; Fraser, D. T., and Fraser, C. J.: Immunisation contre la diphtérie au moyen de l'anatoxine, Ann. Inst. Pasteur **43**: 124 (Jan.) 1929.

10. Fraser, D. T.: Diphtheria Toxoid: A Review, Canad. Pub. Health J. **30**: 469 (Oct.) 1939.

Dividing the groups to show the result of the first Schick test after three doses of toxoid according to the interval between the first and the last dose (immunizing interval) and the interval between the third dose and the test yields a complicated table, and the figures become rather small. In general, there is no marked variation in the percentages of positive reactions obtained, which is in keeping with our previous observation that, so far as Schick testing shows, the immunizing interval can be varied within fairly wide limits without interfering with the results.[1]

The percentages of positive reactions obtained in relation to the total amounts of toxoid administered are shown in table 9. The various subgroups are too small for comparative purposes. The percentages for the group of 731 children given 2 cc. in three doses (0.5; 0.5; 1.0) may be compared with those for the group of 569 children given 2.5 cc. (0.5; 1.0; 1.0); 4.5 per cent of the former and 3.7 per cent of the latter had positive reactions. Whatever difference there is is in favor of the larger amount.

CONCLUSIONS

Positive Schick reactions were observed in 14.9 per cent of the children who were tested from five to eleven years after the third dose of diphtheria toxoid; this is twice the percentage of positive reactions observed four to five years after the third dose of toxoid.

A lower percentage of positive Schick reactions was demonstrated in children who had received a previous test than in those who had not only for the first five years after the third dose of toxoid.

In none of the children did the Schick reactions revert from negative to positive in less than two years after the third dose of toxoid.

The Schick reactions of 8.4 per cent of the children reverted from negative to positive in a period varying from two to ten years.

Diphtheria toxoid administered to infants 6 months old achieved immunization which, as gaged by the Schick test, is as lasting as that which follows its administration to older children.

It would seem advisable to give all children who receive three injections of diphtheria toxoid in infancy either a Schick test at the age of 5 years and, if the reaction is positive, a further subcutaneous injection of 1 cc. of toxoid or, if the test is omitted, the dose of toxoid at this age, which corresponds usually with their entrance into school.

THE OLFACTORY BULBS IN HUMAN POLIOMYELITIS

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CINCINNATI

It was shown in a previous report [1] that in experimental poliomyelitis one or both of the olfactory bulbs exhibited characteristic pathologic changes, that is, neuronal necrosis, neuronophagia and perivascular and meningeal cellular infiltration, when the virus invaded the nervous system by the olfactory pathway but not after invasion by other pathways (subcutaneous, intrasciatic, intraocular, tonsillopharyngeal and intracerebral). Despite the fact that in recent years there has been a strong tendency to regard the olfactory pathway as the usual portal of entry for the virus in man, there is actually no direct evidence for such an assumption. It was, therefore, desirable to determine whether or not the olfactory bulbs in human poliomyelitis showed changes similar to those found in experimental poliomyelitis which was induced by nasal instillation of the virus.

Smith's [2] report, in 1934, on 56 olfactory bulbs from about 40 cases was inconclusive, partly because the statement that "in less than a fourth of them do the characteristic cellular infiltrative changes, as seen in the ganglia and nerve roots, appear" failed to indicate whether or not there was neuronal damage, and also because in the majority of cases only a single bulb was examined. Unfortunately, it was not possible to reexamine Smith's material in the light of the observations in experimental poliomyelitis, because the sections and blocks had been lost.[3] In 1935, Horányi-Hechst [4] reported that the olfactory bulbs were free from change in 15 cases, and in 1937 Harmon [5] referred to the absence of pathologic

From the Laboratories of the Rockefeller Institute for Medical Research, New York.

1. Sabin, A. B., and Olitsky, P. K.: Olfactory Bulbs in Experimental Poliomyelitis: Their Pathologic Condition as Indicator of Portal of Entry of Virus, J. A. M. A. **108**:21 (Jan. 2) 1937.

2. Smith, L. W., in Landon, J. F., and Smith, L. W.: Poliomyelitis: A Handbook for Physicians and Medical Students, Based on a Study of the 1931 Epidemic in New York City, New York, The Macmillan Company, 1934, p. 50.

3. Smith, L. W.: Personal communication to the author.

4. Horányi-Hechst, B.: Zur Histopathologie der menschlichen Poliomyelitis acuta anterior, Deutsche Ztschr. f. Nervenh. **137**:1, 1935.

5. Harmon, P. H., in discussion on Toomey, J. A.: Active and Passive Immunity and Portal of Entry in Poliomyelitis, J. A. M. A. **109**:402 (Aug. 7) 1937.

change in olfactory bulb material from 9 cases. Harmon's material, which he sent to me for study, consisted of sections through the olfactory tracts and of small pieces mostly from the center of the olfactory bulbs, areas which never show any pathologic change even in cases of the severest experimental poliomyelitis.

It was obvious that in order to be able to make any statement about the human olfactory bulbs it was necessary to have (1) perfect specimens, preferably both bulbs from each subject cut partially or completely in serial sections, and (2) evidence of definite, pathologic change elsewhere in the nervous system, consistent with a diagnosis of poliomyelitis. Such material became available through Dr. Paul H. Harmon during the 1937 epidemic in Chicago, as a result of the cooperation of Drs. Herman N. Bundesen, Archibald Hoyne and Victor Levine. Dr. Harmon furnished the clinical histories, and Dr. Levine sent me sections of the spinal cord, medulla and other regions of the nervous system in each case. Both olfactory bulbs were available in 9 cases and a single bulb in a tenth case. Some of the bulbs were fixed in a solution of formaldehyde and others in Zenker's solution prepared with 5 per cent glacial acetic acid. Partial serial sections (every other five or six sections in a ribbon were retained) were cut at 7 microns in the sagittal plane and were stained with Giesma's stain, with Lillie and Pasternack's modification (using buffered solutions) of the Romanowsky stain for formaldehyde-fixed tissues,[6] with hematoxylin and eosin or with hematoxylin and phloxine. More than 2,000 sections of olfactory bulbs were thus available for examination.

Although the essential results of this study have already been referred to in several communications,[7] they have not hitherto been reported in detail, because it was desirable to integrate the studies on the olfactory bulbs with the observations elsewhere in the nervous system and with the clinical histories. Six olfactory bulbs from 3 other subjects were studied less completely. In the meantime, several other reports appeared on the condition of the olfactory bulbs in human poliomyelitis. De Groat[8] found no change in the olfactory bulbs from 3 patients who

6. Lillie, R. D., and Pasternack, J. G.: Romanowsky Staining with Buffered Solutions: Current Modification, J. Tech. Methods **15**:65, 1936.

7. Sabin, A. B.: Portal of Entry and Transmission of Poliomyelitis Virus, Internat. Bull. Econ. M. Research & Pub. Hyg. **A40**:45, 1939. Harmon, P. H.: Geographical and Racial Incidence of Poliomyelitis, ibid. **A40**:148, 1939. King, L. S.: Some Problems in Pathology of Neurotropic Viruses, J. A. M. A. **113**: 1940 (Nov. 25) 1939.

8. De Groat, A. F.: Observations on Pathology and Pathogenesis of Poliomyelitis, South. M. J. **31**:475, 1938.

died in the 1937 outbreak in Arkansas, and Stillerman and Fischer [9] reported that the olfactory bulbs were normal in a patient in whom poliomyelitis developed after removal of the tonsils and adenoids. Swan [10] studied serial sections of the olfactory bulbs in 4 cases which occurred in the 1937-1938 epidemic in South Australia, and Robertson [11] reported on serial sections of the olfactory bulbs from 11 cases occurring in the 1937 epidemic in Victoria, Australia, but neither of them found significant lesions.

RESULTS

The essential data in the 10 cases occurring in the 1937 Chicago epidemic are listed in the table. The primary paralysis was bulbar in type in 5 cases, bulbar and spinal in 2 and spinal in 3; terminally, there was clinical evidence of involvement of the cranial nerves in all but 1 case. There were definite lesions, both neuronal and infiltrative, in the spinal cord and medulla in all cases. The extensive lesions in the medulla affecting especially the nuclei of the ninth and tenth cranial nerves were comparable to those seen in monkeys infected by the tonsillopharyngeal route, rather than to the scattered mild changes usually observed in the medulla of monkeys in which the virus invaded along the olfactory pathway. No pathologic change was found in approximately 2,000 sections of 18 of the 19 bulbs examined. In 15 of 90 sections from the remaining bulb, perivascular infiltration with a single row of round cells and an occasional polymorphonuclear leukocyte were found around a single vessel in the section; this was not associated with any neuronal change and was in no way comparable even to the mildest changes in the specifically affected olfactory bulbs in experimental poliomyelitis. Furthermore, it is well known that meningeal and perivascular infiltrations are a reaction to, rather than the result of, direct virus action and can extend far beyond the location of neuronal lesions specifically caused by the virus. In the 104 sections of the olfactory bulbs from the 3 cases not included in the table, there was also no pathologic change. These results on material from the 1937 Chicago epidemic are in striking agreement with Robertson's observations [11] on the serial sections of 20 bulbs from 11 patients in the 1937 epidemic in Australia (Victoria), in which he found that only one bulb (and that from a case of the bulbar type) revealed any abnormality. Robertson described the abnormality as follows:

> Here there was an intense accumulation of lymphocytes around one vessel running vertically towards the surface and around its large tributaries. Near this vessel

9. Stillerman, M., and Fischer, A. E.: Acute Bulbar Poliomyelitis Following Recent Tonsillectomy and Adenoidectomy, Am. J. Dis. Child. **56**:778 (Oct.) 1938.

10. Swan, C.: Anatomical Distribution and Character of Lesions of Poliomyelitis, Australian J. Exper. Biol. & M. Sc. **17**:345, 1939.

11. Robertson, E. G.: Examination of Olfactory Bulbs in Fatal Cases of Poliomyelitis, M. J. Australia **1**:156, 1940.

Condition of the Olfactory Bulbs in Human Poliomyelitis in Relation to Type of Disease and Pathologic Changes Elsewhere in Nervous System *

Case Number	Age of Patient, Years	Days Between Onset of First Symptoms and Death	Primary Paralysis		Terminal Paralysis		Lesions					Olfactory Bulbs			
							Spinal Cord			Medulla		1		2	
			Spinal	Bulbar	Spinal	Bulbar	Lumbar Portion	Thoracic Portion	Cervical Portion	Level and Chief Zone Affected	Pathologic Changes	Number of Sections	Pathologic Changes	Number of Sections	Pathologic Changes
77	9	7	0	+ (IX, X)	0	+ (VII, IX, X)	N+++ P+++	N+++ P+++	....	Rostral end inferior olive (R. F., X)	N++++ P++++	62	None	..	.....
80	10/12	7	+ (L, U)	?	+	+ (X)	N++++ P++	N++++ P+++	....	Caudal end inferior olive at closure of 4th ventricle	N+ P++	94	None	65	None
82	13	10	+ (U)	0	+ (U, L?)	+ (VII, IX, X)	N+++ P+++	..... P+++	N++++ P+	Caudal end inferior olive at closure of 4th ventricle	N+ P+	188	None	196	None
86 (S. T.)	13	10	+ (U)	+ (IX, X)	+ (U, L)	+ (IX, X)	N++++ P++++	N++ P++++	N++++ P++++	Rostral end inferior olive (IX, X)	N++ P++	54	None	52	None
88 (S. T.)	33	11	0	+ (IX, X)	+ (Intercostal area)	+ (IX, X, XII, III)	N++ P++	N++ P++	N+++ P+++	Rostral end inferior olive (R. F. IX, X) Decussation of pyramids	N+++ P++ N+ P++	67	None	102	None
90	8	7	0	+ (VII, IX, X)	0	+ (VII, IX, X)	N++ P++	N+ P+	N++ P+++	Rostral end inferior olive (R. F.) Decussation of pyramids (nucleus gracilis)	N++++ P++ N+++ P++	148	None	139	None
92 (S. T.)	14	9	+ (U)	+ (VII, IX, X)	+ (U)	+ (VII, IX, X)	N++ P++	N++ P++	N++++ P++	Caudal end inferior olive (R. F.)	N++ P++	96	None	143	None
94	16	5	0	+ (IX, X)	+ (U?)	+ (IX, X)	N++ P++	N++ P++	N+++ P++	Middle of inferior olive (R. F.)	N+++ P+++	104	None	130	None
95	18	5	+ (urinary bladder)	0	+ (U, L?)	0	N++ P++	N++ P++	N+++ P++	Middle of inferior olive (R. F.)	N+++ P++	105	None	90	See note †
97	5	3	0	+ (IX, X)	0	+ (IX, X)	..... P+	..... P+	N++ P++	Caudal end inferior olive (R. F., N. cun., N. gr. Maon)	N++ P++	102	None	134	None

* N = neuronal necrosis, neuronophagia; +, few cells involved; ++++, involvement of an entire zone.
P = perivascular round cell infiltration; +, occasional vessel affected; +++, large number of vessels affected.
U = upper extremities; L = lower extremities. (IX, X), etc., indicates involvement of ninth, tenth, etc., cranial nerves.
R. F. = reticular formation. N. gr. indicates nucleus gracilis; N. cun., nucleus cuneatus; Maon, medial accessory olivary nucleus.
S. T. = History of sore throat.

† Sections 1 to 6, negative; 7 to 11, one vessel in glomerular layer surrounded by single row of round cells and an occasional polymorphonuclear cell but no cytlosis

were a few small focal accumulations of lymphocytes. Damage to nerve cells was not evident and certainly did not involve any of the groups of large mitral cells.

Although the clinical course of 9 of the 11 patients was characterized by early development of pharyngeal and respiratory paralysis, the olfactory bulbs of the 2 patients with spinal paralysis were equally without change. In 3 of the 4 patients whose olfactory bulbs were studied in serial section by Swan [10] the initial paralysis was spinal in origin, but no pathologic change was found in any of them.

COMMENT

When the results of the present study are combined with those of Robertson [11] and Swan,[10] one finds that 49 olfactory bulbs from 26 cases of human poliomyelitis (occurring in 1937) have been studied in partial or complete serial sections without any pathologic change being observed comparable to that which can be found in random sections of the olfactory bulbs of monkeys succumbing after nasal instillation of poliomyelitis virus. The perivascular infiltration found around an occasional vessel in 2 of the 49 bulbs, unassociated with any evidence of neuronal damage, cannot in itself be accepted as evidence of the presence or passage of virus through those bulbs.

The question raised by these observations is whether or not the absence of lesions in the olfactory bulbs indicates the absence of virus, and, therefore, definitely rules out the olfactory route as the portal of entry of the virus in man. The answer to this question is that the absence of lesions does not necessarily indicate the absence of virus, although it is noteworthy that, in general, practically all the sites in which lesions have been found in experimental poliomyelitis in the monkey have also been found to be involved in man (Smith,[2] Horányi-Hechst,[4] De Groat,[5] Swan [10] and my personal observations). Schultz and Gebhardt [12] have shown that in monkeys infected by the nasal route the virus may be present in almost as high a concentration in some of the higher centers of the brain as in the spinal cord, with great destruction of nerve cells in the latter and little or no damage in the former. Although I have found evidence of neuronal damage in random sections of those higher centers, such as the olfactory bulbs, the anterior perforated space, the hypothalamus and the thalamus, in monkeys succumbing after nasal instillation of virus, it is true that the number of cells affected is usually only a small fraction of those found damaged in the cord. The total absence of obvious neuronal damage in serial sections of the human olfactory bulbs, however, suggests either that these struc-

12. Schultz, E. W., and Gebhardt, L. P.: Relation of Concentration of Virus to Pathogenesis of Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **40**:577, 1939.

tures possess a refractoriness not found elsewhere in the human nervous system or that they are not primarily affected by the virus.

It is clear, therefore, that what one needs to know is whether or not the virus of poliomyelitis can be demonstrated in the olfactory bulbs of human subjects in whom the spinal cord and medulla are proved to be infective.[12a] The absence of virus from the olfactory bulbs under these circumstances would be strong evidence against the olfactory route as the portal of entry, although the presence of virus could not be accepted as evidence for it. Although it has been shown that in 7 of 8 rhesus monkeys infected by the tonsillopharyngeal route [13] the olfactory bulbs contained no virus, one cannot as yet exclude the possibility that there may be a greater centrifugal spread of virus in man than in the rhesus monkey. It has been found, for example, that in man rabies virus entering by the nerves supplying the hand could be demonstrated in appreciable amounts in the olfactory bulbs at death.[14] Until more is known of the centrifugal spread of poliomyelitis virus in man, it is equally difficult to interpret the significance of the presence of virus in secretions of the upper part of the respiratory tract, in the nasal mucosa, in the tonsils and in the feces. At present there is, therefore, no direct evidence for or against the belief that any particular site is the portal of entry of the virus in man.[12a]

SUMMARY

Examination of 25 olfactory bulbs (21 in partial serial sections) from 13 cases of human poliomyelitis did not reveal the pathologic changes which have been observed in the olfactory bulbs of monkeys succumbing after nasal instillation of poliomyelitis virus. A review of the existing data reveals that there is at present no direct evidence for or against the belief that any particular site is the portal of entry of the virus in man.

12a. In a recent study, the results of which have not been published, A. B. Sabin and R. Ward found no virus in the olfactory bulbs from 5 cases of human poliomyelitis in which the virus was isolated from other tissues. These findings can be considered as strong evidence against the theory that the olfactory pathway is the usual portal of entry of the virus in man.

13. Sabin, A. B.: Experimental Poliomyelitis by Tonsillo-Pharyngeal Route, with Special Reference to Influence of Tonsillectomy on Development of Bulbar Poliomyelitis, J. A. M. A. **111**:605 (Aug. 13) 1938.

14. Sabin, A. B., and Ruchman, I.: Spread of Virus in an Unvaccinated Case of Human Rabies, Proc. Soc. Exper. Biol. & Med. **44**:572, 1940.

ROENTGENOLOGIC STUDY OF ANOMALIES OF THE HANDS IN ONE HUNDRED CASES OF MONGOLISM

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The clinical entity of mongolism was described by Down [1] in 1866. The disease is characterized by mental retardation and somatic changes involving many parts of the skeleton. The typical appearance of the head and face is probably due not to an atavistic reversion to mongolian features but rather to an abnormal underdevelopment of the bony structures at the base of the skull (Benda [1a]). Other anomalies found in persons with mongolism are undersized stature, slanting eyes, small and flattened nose, small and poorly shaped ears, thick lips, scrotal tongue, delay in dentition, lax joints, congenital heart disease and occasionally other signs of maldevelopment.

A peculiarity in the shape of the hand of mongolian imbeciles was described first by Smith [2] in 1896. He called attention to a marked outward bowing or curve of the little finger. A roentgenogram demonstrated for the first time the reason for his clinical impression. From it he saw that the second phalanx of the little finger was considerably shorter than normal and that there was much lateral displacement of the terminal phalanx. He found this curve of the little finger in nearly every case of mongolian idiocy and expressed the opinion that it might almost be looked on as one of the constant peculiarities of this disease. West [3] disputed the observations of Smith and found some degree of curving of the fifth finger in many normal children. Koplik [3a] agreed that many normal people show a small bend in their fingers. Siegert [4] stated in 1910 that the second phalanx of the

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1. Down, J. L.: Observations on an Ethnic Classification of Idiots, Clin. Lect. & Rep. London Hosp. **3**:259-262, 1866; cited by Smith.[2]

1a. Benda, C. E.: Studies in Mongolism, Arch. Neurol. & Psychiat. **41**:83-97 (Jan.) 1939.

2. Smith, T. T.: A Peculiarity in the Shape of the Hand in Idiots of the Mongol Type, Pediatrics **2**:315-320, 1896.

3. West, J. P.: A Note on the Little Finger of the Mongolian Idiot and of Normal Children, Arch. Pediat. **18**:918-924, 1901.

3a. Koplik, in discussion on West.[3]

4. Siegert, F.: Der Mongolismus, Ergebn. d. inn. Med. u. Kinderh. **6**:565-600, 1910.

fifth finger is hardly ever normal in mongolian idiots. Muir [4a] found the curving of the fifth finger in 12 of 26 cases. Schinz [5] stated in his textbook on roentgenology that the anomaly of the middle phalanx of the fifth finger is commonly found in newborn babies with mongolism. Köhler [6] mentioned the shortening and deformity of the phalanx; he also stated that the same appearance is found occasionally in persons with progressive myositis ossificans and psoriasis and sometimes also in normal children. While Benda [1a] had roentgenograms of the hands of 29 persons with mongolism, he stated nothing about the anomaly of the fifth finger. Werner, Lewald, Johns and Kelling [7] mentioned the anomaly of the fifth finger in their report. Warner,[8] in a review of 100 cases, mentioned the peculiar deformity of the fifth finger as a specific feature of mongolism and the most constant of the congenital deformities. She stated that it may also be found as a dominant hereditary character apart from mongolism.

Other anomalies are the presence of a center of ossification at the distal end of the first metacarpal bone and notching at the proximal end of the second metacarpal bone. These are supposed to be expressions of a delayed growth of bone, and the failure of these extra epiphysial nuclei to appear in normal persons is explained osteogenetically on the ground that a proximal nucleus is always present but that the ossifying diaphysis reaches it before it has time to attain an independent formation (Warner). These nuclei usually appear between the sixth and the eighth year. This occurrence has been noted as more or less typical by Werner, Köhler, Schinz and Siegert. The fact is mentioned by some authors that these abnormal epiphyses may be seen also in myxedema.

There is considerable divergence of opinion as to whether the osseous development is delayed, advanced or normal in cases of mongolism. Kassowitz [9] could not demonstrate a delay in ossification, as in athyreosis. Siegert found the osseous age usually normal; he noted at times premature or delayed ossification. Bullard [9a] found distinct retardation in

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4a. Muir, J.: An Analysis of Twenty-Six Cases of Mongolism, Arch. Pediat. **20**:161-169, 1903.

5. Schinz, H. R.: Lehrbuch der Roentgen-Diagnostik, Leipzig, Georg Thieme, 1928.

6. Köhler, A.: Röntgenology: The Borderlands of the Normal and Early Pathological in the Skiagram, ed. 2, translated by A. Turnbull, Baltimore, William Wood & Company, 1935.

7. Werner, A. A.; Lewald, J.; Johns, G. A., and Kelling, D.: Growth in Children with Mongolism, Am. J. Dis. Child. **57**:554-563 (March) 1939.

8. Warner, E. N.: A Survey of Mongolism with a Review of One Hundred Cases, Canad. M. A. J. **33**:495-500, 1935.

9. Kassowitz, K.: Infantiles Myxödem, Mongolismus und Mikromelie, Wien. med. Wchnschr. **42**:1049, 1105, 1155, 1202, 1256, 1301, 1357, 1409 and 1452, 1902.

9a. Bullard, W. N.: Mongolian Idiocy, Boston M. & S. J. **164**:56, 1911.

25 patients of whom he had roentgenograms. Clift [9b] also found delay and irregularity in dentition. Schinz noted the late or irregular appearance of the epiphysial nuclei. In Köhler's opinion the differentiation of the osseous nuclei is partly delayed, partly accentuated and partly normal. In Benda's cases the first appearance of the centers of ossification of the carpal bones was often premature; normal osseous age was found, but retardation was not noted. That the appearance of bony nuclei may be slightly delayed or normal was stated by Werner and his associates. They asserted that osseous development was generally retarded. Brousseau [9c] found an irregularity in the time of ossification.

All authors agree on the general appearance of the hands. They are much shorter and broader than normal. The tips of the fingers are usually slender.

Fig. 1.—Anomalous short, deformed middle phalanx of the fifth finger.

The present investigation was undertaken on 100 typical mongolian imbeciles.[10] Whenever there was a question as to the clinical diagnosis the patient was not examined roentgenologically. The ages of the patients ranged from 2 months to 46 years; there were 72 children (between 2 months and 15 years of age) and 28 adults (above 15 years).

9b. Clift, M. W.: Roentgenological Findings in Mongolism, Am. J. Roentgenol. **9**:420-422, 1922.

9c. Brousseau, K.: Mongolism: A Study of the Physical and Mental Characteristics of Mongolian Imbeciles, Baltimore, Williams & Wilkins Company, 1928.

10. The children examined were from the Milwaukee Children's Hospital, the St. Coletta School for Feebleminded, Jefferson, Wis., and the Southern Colony for Feebleminded, Union Grove, Wis. Some were patients of Dr. M. G. Peterman, of Milwaukee.

Of these 100 patients, 33 showed no roentgen evidence of any anomalies in the bones of the hands. In 67 there was evidence of some bony abnormality. In most of them (62 patients) the anomaly observed was the shortening or deformity of the middle phalanx of the fifth finger (fig. 1), which, when present, was always bilateral. In most of these patients there was only shortening, sometimes extreme, sometimes slight. At times the phalanx was almost rectangular, at times triangular. Rarely were there two centers of ossification forming the phalanx. If the deformity of the middle phalanx was marked, there was usually a

Fig. 2.—Anomalous so-called pseudoepiphyses at the distal end of the first metacarpal and at the proximal end of the second metacarpal bone.

pronounced curving of the fifth finger. Only in a few cases was there subluxation of the terminal phalanx or great deformity of the middle phalanx.

Forty-three of the 62 patients with an abnormal middle phalanx of the fifth finger showed more or less curving of this finger. The roentgenologic interpretation of the curving is not always easy because it is difficult not to mistake a possible slight curve due to the projection of the not always completely flat position of the finger on the cassette. In 30 of the 62 patients with the abnormality in the middle phalanx of the fifth finger there were other associated anomalies, consisting of notching or a separate epiphysis at the base of the second metacarpal

bone, in 23 patients, or an abnormal center at the distal end of the first metacarpal bone, in 10 patients (fig. 2). In 5 patients there was one of these anomalies without malformed fifth finger.

It is of interest that of the 72 children up to 15 years of age, 53 (73 per cent) showed congenital anomalies, while only 19 (27 per cent) had normal bony structures. In the series of 28 adults with mongolism, 14 (50 per cent) were normal and 14 (50 per cent) exhibited evidence of abnormal bone structure. While the incidence of the shortened and deformed middle phalanx of the fifth finger was somewhat less in adults, there was complete absence of the abnormalities in the first and second metacarpal bones, which, apparently, may only be seen in the hands of growing children.

The development of the hands and wrists was determined roentgenologically by comparing the films with those of normal subjects in Todd's [10a] atlas. Results of previous investigations seem to be, at times, somewhat inconclusive because of the lack of standards. The osseous age of 57 (79 per cent) of the 72 children up to 15 years of age was normal, which is therefore the rule for children with mongolism. Of 15 patients, there were a slight advance in osseous development in 10 (14 per cent) and a slight delay in 5 (7 per cent). Neither the advance nor the delay in osseous development was marked in any patient.

The length of the hand was measured from the tip of the middle finger to the medial aspect of the distal end of the radius. In practically all cases the hands were from 10 to 30 per cent shorter than normal hands as reproduced by Todd.

During the course of this investigation (about two years) a few roentgenograms of the hands of apparently healthy children were seen which showed the abnormalities that have been described. Their appearance was identical with that of the hands showing the developmental anomalies of the bones characteristic of mongolian idiocy. The rate of occurrence of the abnormalities was probably about 1 in 500. In a few other conditions the same abnormalities were noted: nonmongolian imbecility, multiple congenital anomalies and myxedema.

CONCLUSIONS

An anomalous middle phalanx of the fifth finger was found in 62 of 100 cases of mongolian idiocy; in 30 cases other anomalies, mainly so-called pseudoepiphyses of the first and second metacarpal bones, were present. Of the children with mongolism 73 per cent showed some abnormality in the bones of the hand.

The osseous development was normal in 79 per cent of the children, advanced in 14 per cent and delayed in 7 per cent.

10a. Todd, T. W.: Atlas of Skeletal Maturation, St. Louis, C. V. Mosby Company, 1937.

MINIMAL NITROGEN REQUIREMENTS OF CHILDREN WITH THE NEPHROTIC SYNDROME

EFFECT OF THE ADMINISTRATION OF A GROWTH-PROMOTING ANTERIOR PITUITARY EXTRACT

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NEW YORK

The appetite of patients with the nephrotic syndrome is notoriously poor. In addition to lacking a desire for food these patients are peculiarly subject to gastrointestinal upsets, which may be induced or exacerbated by forced feeding. It is especially important that nephrotic patients be maintained in nitrogen equilibrium to offset the severe malnutrition characteristic of the syndrome.

Previous studies from this clinic on the capacity of nephrotic children similar in age to those used in this study to assimilate dietary protein indicated that maximum assimilation of nitrogen occurred with a diet containing 3.2 Gm. of protein per kilogram of ideal body weight (accepted average weight for height and age) when the caloric intake was liberal.[1] No data were available regarding the ability of nephrotic children to maintain themselves in nitrogen equilibrium on minimum caloric and nitrogen intakes. Unpublished observations on the incidence of nephrotic crises, with and without accompanying infection of the blood stream and peritoneum, showed a markedly greater morbidity and mortality in crises when the children were fed diets containing less than 2.5 Gm. of protein per kilogram than when the diets contained from 2.5 to 3.5 Gm. of protein per kilogram of ideal body weight. The incidence of crises could be correlated only with nitrogen intake and not with caloric intake. The present study was designed to obtain data on the results of low nitrogen and caloric intakes and, in addition, to test the effect of administration of a growth-promoting extract of the anterior lobe of the beef pituitary on the nitrogen requirements of these patients.

MATERIAL AND METHODS

Studies of nitrogen balance of 6 children with the nephrotic syndrome in the wards of the hospital were made for eight consecutive weeks. Four of these children were girls and 2 were boys. Their ages varied from 2½ to 7 years. Selected clinical and laboratory data on these patients after admission to the hospital are shown in charts 1 to 6. During the period of study the children fortunately were

From the Hospital of the Rockefeller Institute for Medical Research.

1. Farr, L. E.: The Assimilation of Protein by Young Children with the Nephrotic Syndrome, Am. J. M. Sc. **195**:70 (Jan.) 1938.

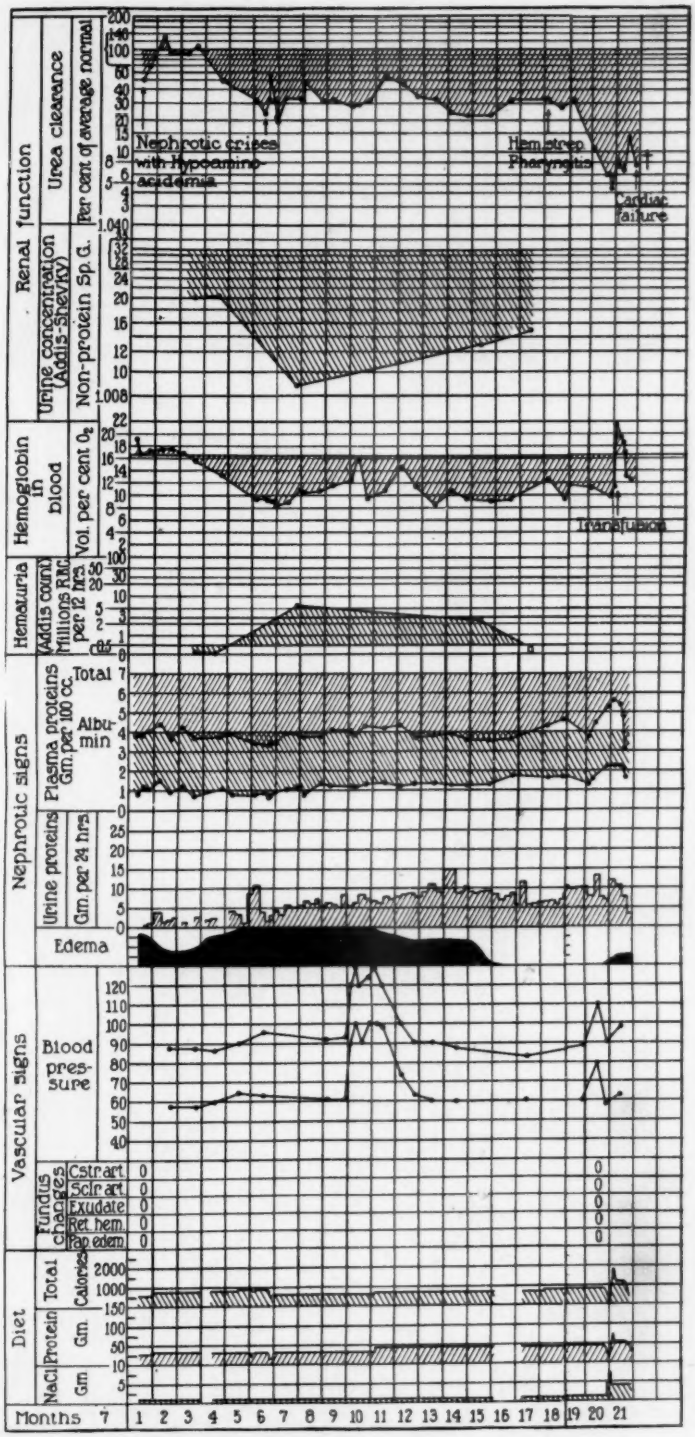

Chart 1.—Data summarizing clinical and laboratory observations on G. B. Illness began seven months prior to admission. The onset was insidious. The present study was carried out during months 8 and 9 of her hospital course. At the age of 3½ years the height was 97 cm. and the ideal weight 15 Kg. At 4 years the height was 98 cm. and the ideal weight 15.5 Kg.

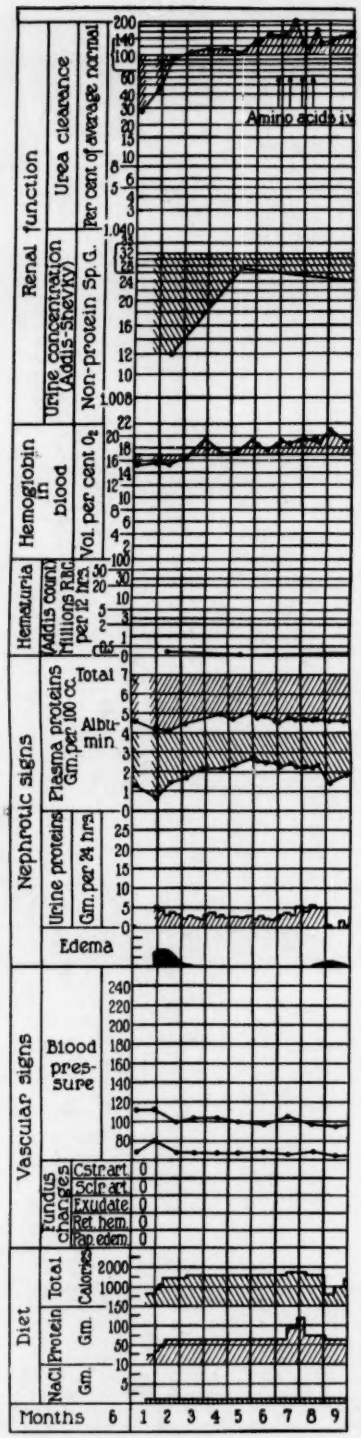

Chart 2.—Data summarizing clinical and laboratory observations on R. Q. Illness began six months prior to admission. The onset was insidious. The present study was carried out during months 3 and 4 of her hospital course. At the age of 6¾ years the height was 123.5 cm. and the ideal weight 24.4 Kg.

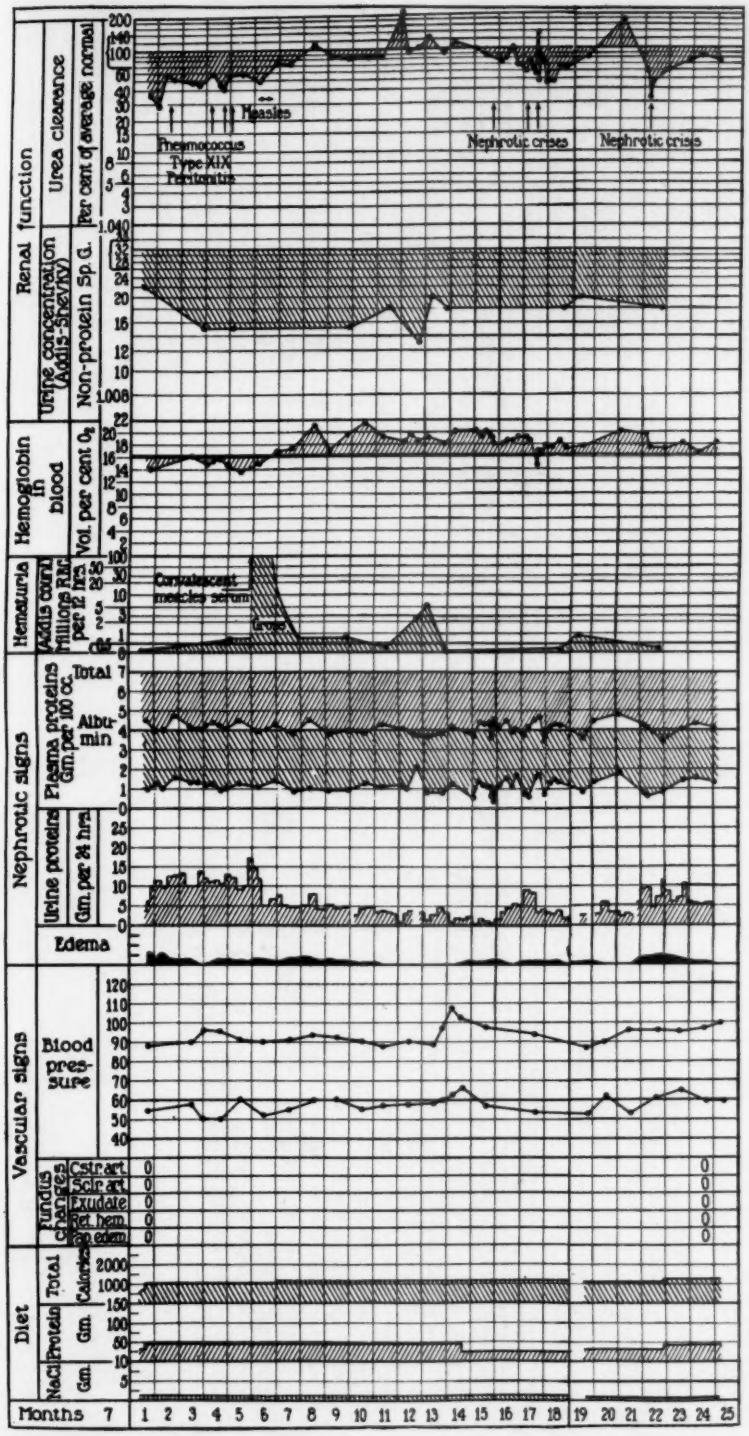

Chart 3.—Data summarizing clinical and laboratory observations on J. C. Illness began seven months before admission. The present study was carried out during months 23 and 24 of his hospital course. At the age of 4 years the height was 98 cm. and the ideal weight 15 Kg. At 6 years the height was 100.5 cm. and the ideal weight 15.9 Kg.

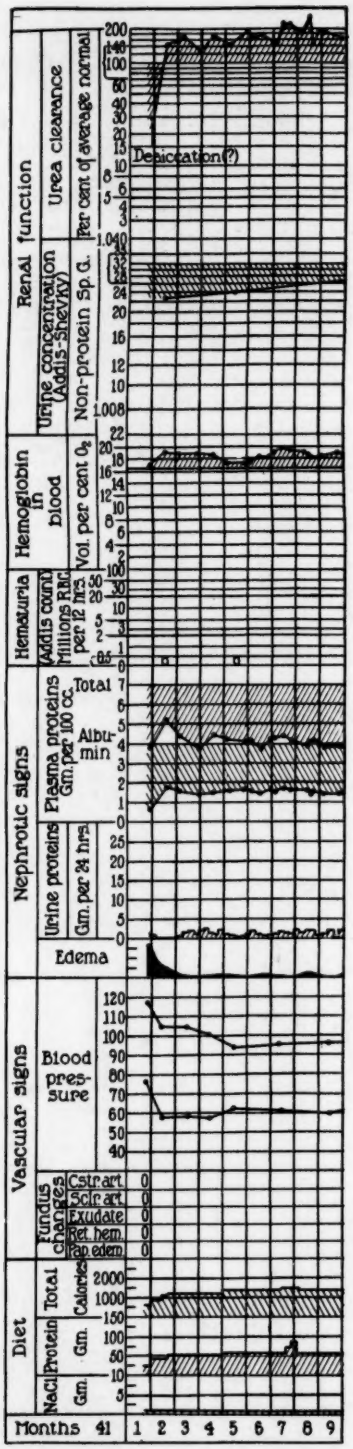

Chart 4.—Data summarizing clinical and laboratory observations on W. O'B. Illness began forty-one months prior to admission. The onset was insidious. The present study was carried out during months 3 and 4 of his hospital course. At the age of 4½ years the height was 108.5 cm. and the ideal weight 18.6 Kg.

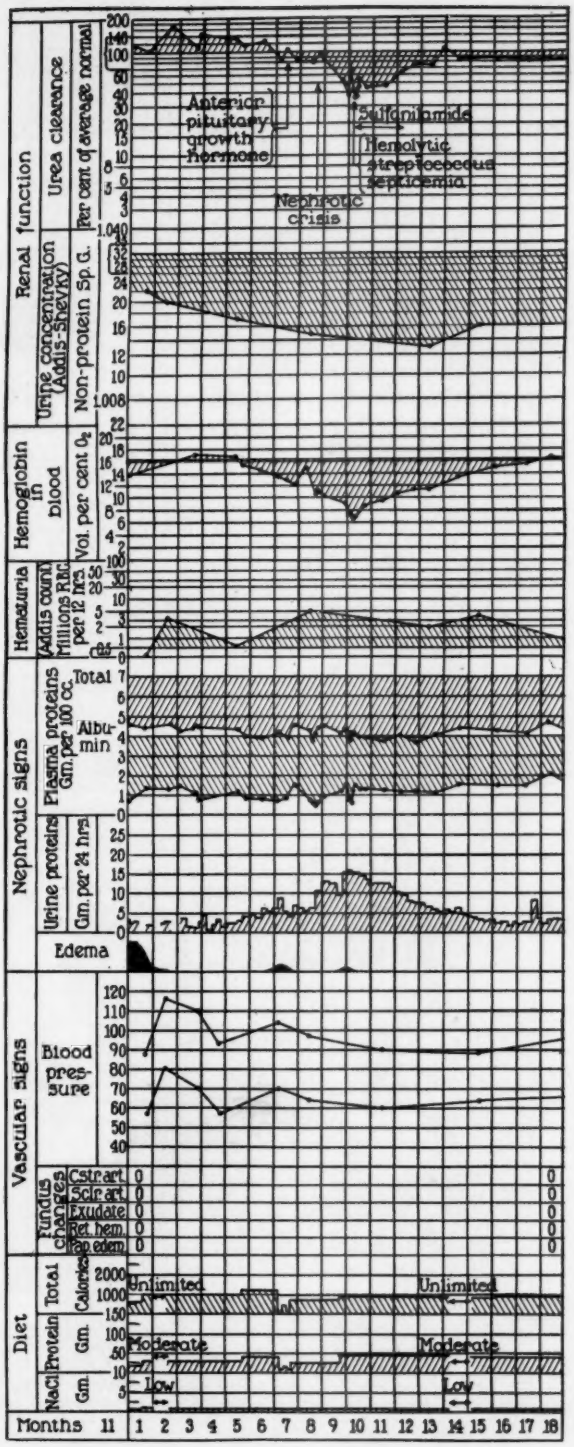

Chart 5.—Data summarizing clinical and laboratory observations on M. G. Illness began two and one half months prior to admission. The onset was insidious. The present study was carried out during months 6 and 7 of her hospital course. At the age of 4 years the height was 98.5 cm. and the ideal weight 15.5 Kg.

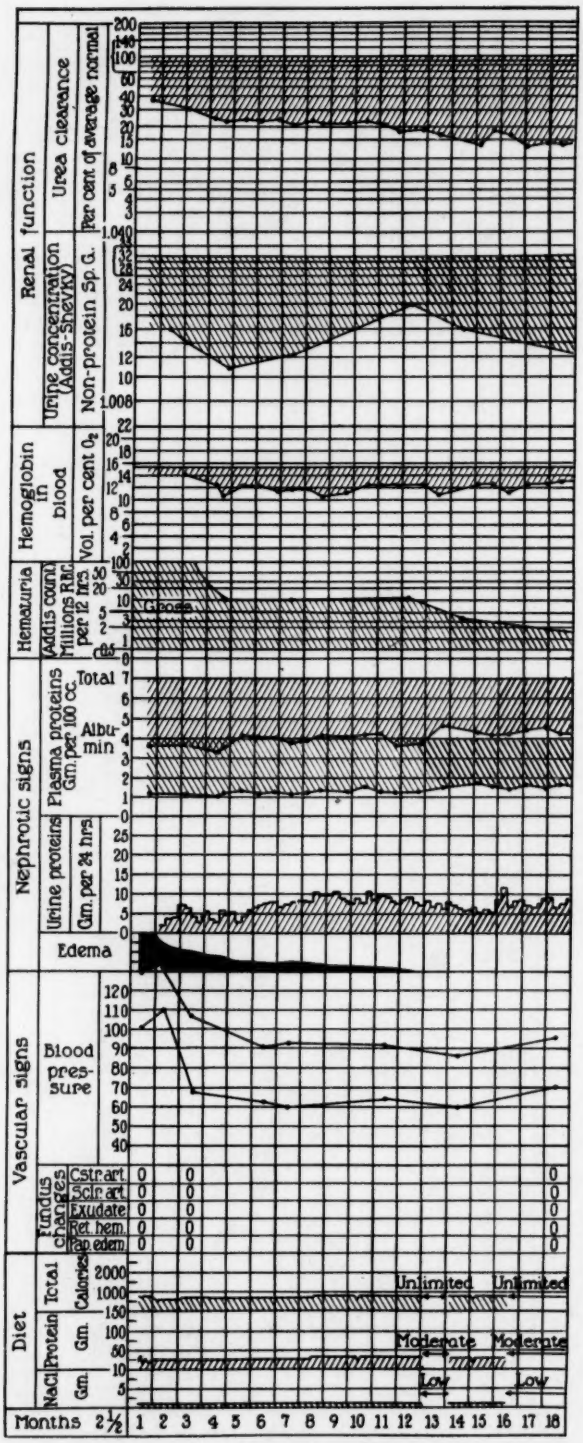

Chart 6.—Data summarizing clinical and laboratory observations on S. W. Illness began eleven months prior to admission. The onset was insidious. The present study was carried out during months 5 and 6 of her hospital course. At the age of 2⅓ years the height was 86 cm. and the ideal weight 11.8 Kg.

free of febrile episodes and of infection of the upper part of the respiratory tract. During the course of observation 1 patient went on a self-imposed and rigorous fast lasting the greater part of two weeks; thereby was furnished an unusual opportunity to observe the effects of semistarvation in this syndrome. No untoward incidents occurred with any of the other children during the period of observation. Each metabolic period was seven days long except the eighth period, which lasted only six days.

TABLE 1.—*Daily Intake of Protein, Fat and Carbohydrate During Periods of Nitrogen Balance Study*

Patient	Age, Year	Ideal Weight, Kg.	Actual Weight, Kg.	Period	Average Daily Food Intake: Protein, Gm.	Fat, Gm.	Carbohydrate, Gm.	Calories	Protein, Gm. per Kg.	Fat, Gm. per Kg.	Carbohydrate, Gm. per Kg.	Calories per Kg.
J. C.....	6	16.4	18.0	1-8	45	45	45	1,270	2.75	2.75	10.5	77.5
R. Q.....	7	24.4	21.2	1-8	67	67	196	1,650	2.75	2.75	8.0	67.6
W. O'B.....	4	18.6	16.0	1-8	51	51	152	1,272	2.75	2.75	8.2	68.4
G. B.....	4	15.0	18.0	1-8	30	30	53	600	2.0	2.0	3.5	40.0
S. W.....	2½	11.8	11.4	1-8	25	25	94	700	2.1	2.1	8.0	59.3
M. G.....	4½	15.5	16.0	1-5	43	43	151	1,160	2.75	2.75	9.75	74.9
				6								
				(1st-6th day)	43	43	151	1,160	2.75	2.75	9.75	74.9
				(7th day)	..	..	..	.....	..	..	..	..
				7								
				(1st day)	..	..	..	.....	..	..	..	..
				(2d day)	12	12	18	228	0.8	0.8	1.1	14.2
				(3d day)	9	9	18	189	0.6	0.6	1.1	11.8
				(4th day)	13	14	21	262	0.8	0.9	1.3	16.3
				(5th day)	8	8	18	180	0.5	0.5	1.1	11.8
				(6th day)	11	20	56	448	0.7	0.3	3.6	28.0
				(7th day)	1	2	3	34	..	..	..	..
				8								
				(1st day)	½	..	10	42	..	..	..	2.6
				(2d day)	..	..	..	.....	..	..	..	..
				(3d day)	26	26	105	758	1.7	1.7	6.75	49.1
				(4th day)	25	25	94	701	1.7	1.7	6.0	45.2
				(5th day)	25	25	95	705	1.7	1.7	6.0	45.2
				(6th day)	25	25	94	701	1.7	1.7	6.0	45.2

The diet fed in each instance represented the maximum caloric intake by those particular children with low calory diets. The content of the experimental diet was determined after a prolonged period of observation in the hospital. With the exception of the 1 child who fasted for several days, none refused food. Each diet was weighed and prepared individually in the diet kitchen of the hospital under the supervision of Miss M. Rhine. The nitrogen content of the diets was calculated from standard tables on food analysis. Throughout the period of study the same weekly diet was used. This permitted adequate variation in the daily menu and by the use of sufficient control periods provided for a check on any inaccuracies in the calculated composition of the diet. A detailed summary of the constituents of the diets is given in table 1. In addition, each patient received what was believed to be an adequate supply of vitamins, provided in mixed concentrates, and

5 to 10 Gm. of fresh brewers' yeast daily. When the patients were unable or unwilling to eat a diet supplying plentiful calories, the proportion of protein was increased. The relative increase of protein in such a diet was carefully adjusted so there was no sacrifice of palatability. It has been the custom in this clinic to feed nephrotic children a basic diet containing 3 Gm. of protein and 3 Gm. of fat per kilogram of ideal body weight. Carbohydrate is then given to bring the caloric level up to that desired. In unusual circumstances, when a very high calory diet is required, additional calories are provided from fat.

After five weeks of observation 3 of the patients were given intramuscularly each day for one week 1 cc. of growth-promoting extract of the anterior lobe of the pituitary. The remaining 3 patients served as modified controls for the effect of the pituitary extract; in addition, the data on the children who received the growth-promoting factor, collected before and after the treatment periods, were used for comparison.

The child who fasted was given amino acids and dextrose intravenously on several occasions during the second week of her fast. The casein hydrolysate mixture [2] was prepared for use as described elsewhere.[3]

The growth-promoting anterior pituitary extract used in this study was especially prepared for this purpose by Armour and Company, and generous amounts were provided for use. Analyses of the nitrogen content of this extract and results of the potency tests made on it have been previously published.[4]

The samples of urine were collected in clean sterile bottles, and whenever practicable the patient voided directly into the bottle. No preservative was used. At the end of each twelve hour period each bottle was tightly stopped and stored in the ice box until the end of that metabolic interval of study. At this time the specimens of urine were thoroughly mixed, and aliquots were removed for analysis. The stools were collected in clean pots, sent to the laboratory immediately after they were obtained and transferred quantitatively to large pyrex jars containing concentrated sulfuric acid. At the end of each period the acid fecal mixture was thoroughly mixed and made up to convenient volume, and aliquots were removed for analysis. For fecal analyses the beginning of each period was marked by feeding a capsule containing 0.2 Gm. of carmine with breakfast, and the first stool containing carmine was taken as the first specimen of the ensuing period. No laxatives were necessary at any time. Urine contaminated with feces was added to the fecal acid mixture.

Standard macro-Kjeldahl procedures were used for determining total fecal nitrogen and urinary nonprotein nitrogen after the urine had been deproteinized with trichloroacetic acid. Urinary protein nitrogen was determined by a minor modification of the biuret colorimetric procedure of Hiller.[5] Urea plus ammonia nitrogen in the urine was determined by the gasometric hypobromite method of

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2. The casein hydrolysate mixture was furnished by Mead Johnson & Co.

3. Farr, L. E.: The Intravenous Administration of Small Doses of Casein Hydrolysate to Nephrotic Children and Its Effect upon the Nitrogen Balance and Plasma Amino Acid Level, J. Pediat. **16**:679 (June) 1940.

4. Farr, L. E., and Alpert, L. K.: The Effect of Endocrine Extracts on the Amino Acids in the Blood with Incidental Findings on the Blood Sugar and Urea, Am. J. Physiol. **128**:722 (March) 1940.

5. Hiller, A.: Determination of Albumin and Globulin in Urine, Proc. Soc. Exper. Biol. & Med. **24**:385 (Jan.) 1927.

Van Slyke and Kugel.[6] The amino acid nitrogen of the plasma was determined by the ninhydrin–carbon dioxide (triketohydrinden hydrate) method of MacFadyen and Van Slyke.[7] The other clinical chemical analyses were carried out by the methods routinely used in this laboratory.

TABLE 2.—*Data* * *on Nitrogen Balances of Six Patients*

Patient	Period †	Total Nitrogen Intake a, Gm.	Urinary Nonprotein Nitrogen b, Gm.	Urinary Protein Nitrogen c, Gm.	Fecal Nitrogen d, Gm.	Nitrogen Balance a—(b+c+d) Gm.	Urea N + NH_3 N / Urinary Nonprotein N
G. B.....	1	4.800	3.218	0.837	0.806	—0.061	0.79
	2	4.800	3.233	1.024	0.679	—0.136	0.84
	3	4.800	3.635	0.856	0.747	—0.438	0.85
	4	4.800	3.694	1.142	0.699	—0.735	0.87
	5	4.800	3.618	0.816	0.592	—0.226	0.84
	6§	4.800	3.901	1.040	0.671	—0.812	0.86
	7	4.800	3.373	0.976	0.690	—0.239	0.84
	8	4.800	3.703	0.832	0.712	—0.447	0.87
R. Q.....	1	10.720	8.610	0.386	1.100	0.624	0.91
	2	10.720	8.477	0.478	1.105	0.660	....
	3	10.720	8.056	0.438	1.126	1.100	0.89
	4	10.720	8.325	0.411	1.231	0.753	0.88
	5	10.720	7.622	0.546	0.997	1.555	0.87
	6	10.720	8.305	0.608	1.062	0.745	0.86
	7	10.720	8.593	0.432	1.211	0.484	0.89
	8	10.720	8.574	0.560	1.342	0.244	0.87
S. W.....	1	4.000	2.127 ‡	0.818 ‡	1.626 ‡	—0.571	....
	2	4.000	2.080 ‡	0.538 ‡	2.184 ‡	—0.802	....
	3	4.000	1.841 ‡	0.712 ‡	2.426 ‡	—0.979	....
	4	4.000	2.033 ‡	0.957 ‡	2.300 ‡	—1.290	....
	5	4.000	2.323 ‡	1.016 ‡	0.834 ‡	—0.173	....
	6	4.000	2.682	1.056	0.800	—0.538	0.85
	7	4.000	2.222	1.040	0.768	—0.030	....
	8	4.000	2.165 ‡	1.136 ‡	0.869 ‡	—0.170	....
W. O'B.....	1	8.160	7.271	0.176	0.884	—0.172	0.90
	2	8.160	6.864	0.328	0.907	0.061	0.89
	3	8.160	6.011	0.338	0.968	0.843	0.90
	4	8.160	6.834	0.244	0.957	0.125	0.86
	5	8.160	7.461	0.399	0.889	—0.529	0.88
	6	8.160	6.832	0.400	0.800	0.128	0.87
	7	8.160	6.604	0.256	0.876	0.424	0.89
	8	8.160	6.875	0.160	0.915	0.210	0.92
M. G.....	1	6.880	4.234 ‡	0.768 ‡	2.230 ‡	—0.352	0.88
	2	6.880	4.045	0.694	1.263	0.878	0.89
	3	6.880	4.524	0.963	1.142	0.251	0.87
	4	6.880	4.919 ‡	0.824 ‡	1.331 ‡	—0.194	0.88
	5	6.880	4.908 ‡	0.944 ‡	1.178 ‡	—0.150	0.85
	6§	5.897	4.087 ‡	1.392	2.046 ‡	—1.648	0.88
	7	1.234	2.728	1.118	0.409	—3.021	....
	8	4.372	2.260	0.747	1.619	—0.334	0.87
J. C.....	1	7.200	4.184	1.337	0.981	0.698	0.85
	2	7.200	4.258	0.910	1.094	0.943	0.82
	3	7.200	4.771	1.067	1.105	0.257	0.85
	4	7.200	4.505	1.301	1.298	0.096	0.85
	5	7.200	4.759	0.944	1.249	0.248	0.82
	6§	7.200	4.725	0.920	1.088	0.467	0.86
	7	7.200	4.954	0.864	1.164	0.218	0.85
	8	7.200	5.168	0.912	1.233	—0.113	0.87

* Data were calculated as daily averages for each period.

† Period 8 lasted six days; all other periods seven days each. The study ran a total of fifty-five days.

‡ Specimens of urine contaminated with feces were included in totals for stools.

§ A daily intramuscular injection of 1 cc. of growth-promoting anterior pituitary extract was given during this period.

6. Van Slyke, D. D., and Kugel, V. H.: Improvements in Manometric Micro-Kjeldahl and Blood Urea Methods, J. Biol. Chem. **102**:489 (Oct.) 1933.

7. MacFadyen, D. A., and Van Slyke, D. D.: Application of Ninhydrin-Co_2 Method for Determination of Amino Acids to Blood and Urine, to be published.

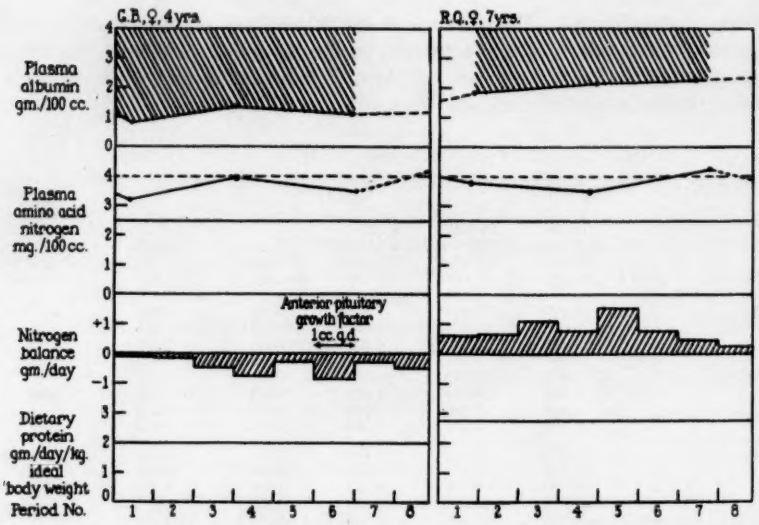
G.B., ♀, 4 yrs.
R.Q., ♀, 7 yrs.
Plasma albumin gm./100 cc.
Plasma amino acid nitrogen mg./100 cc.
Anterior pituitary growth factor 1 cc. q.d.
Nitrogen balance gm./day
Dietary protein gm./day/kg. ideal body weight
Period No.

Chart 7.—Graphic representation of data from studies of nitrogen balance on G. B. and R. Q. Note that R. Q. was in positive nitrogen balance throughout, while G. B. was consistently in negative nitrogen balance. The values for amino acid nitrogen of the plasma in these 2 patients did not show as consistent hypoaminoacidemia as has been generally encountered in nephrotic children of these ages.

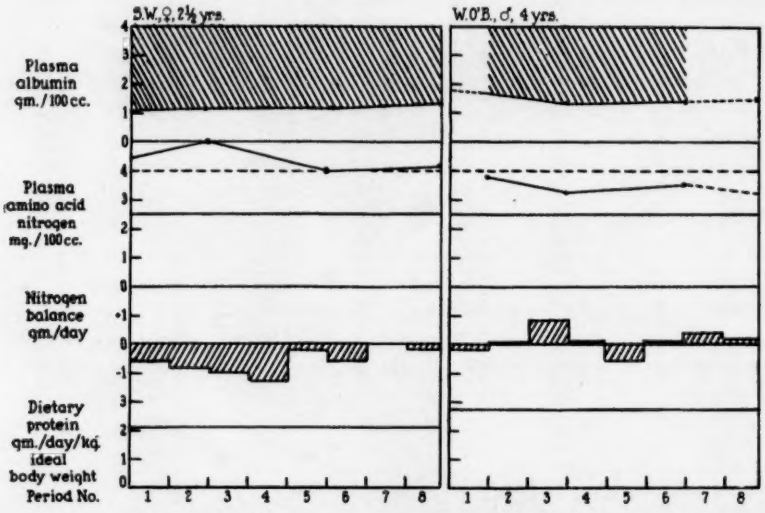
S.W., ♀, 2½ yrs.
W.O'B., ♂, 4 yrs.
Plasma albumin gm./100 cc.
Plasma amino acid nitrogen mg./100 cc.
Nitrogen balance gm./day
Dietary protein gm./day/kg. ideal body weight
Period No.

Chart 8.—Graphic representation of data from studies of nitrogen balance on S. W. and W. O'B. Note that whereas S. W. lost nitrogen throughout the period of study W. O'B. was in positive nitrogen balance for six of the eight periods. The values for plasma amino acid nitrogen for W. O'B. were quite characteristic. There was no apparent explanation for the normal values for plasma amino acid nitrogen seen in S. W. during this period. Such values are more characteristic of patients with pronounced glomerular nephritis than of those with outstanding nephrotic signs but with normal renal function.

Changes of body weight during the periods of study were not of sufficient magnitude to require correction of the observed nitrogen balances.

RESULTS

Data on the nitrogen balances are given in detail in table 2 and are graphically summarized in charts 7 to 9. Of the 4 children fed daily rations containing 2.75 Gm. of protein per kilogram of ideal body weight, 1, R. Q., maintained herself in positive nitrogen balance throughout the eight weeks of study and for the eight periods assimilated a daily average of 0.771 Gm. of nitrogen, or 0.032 Gm. per kilogram of ideal

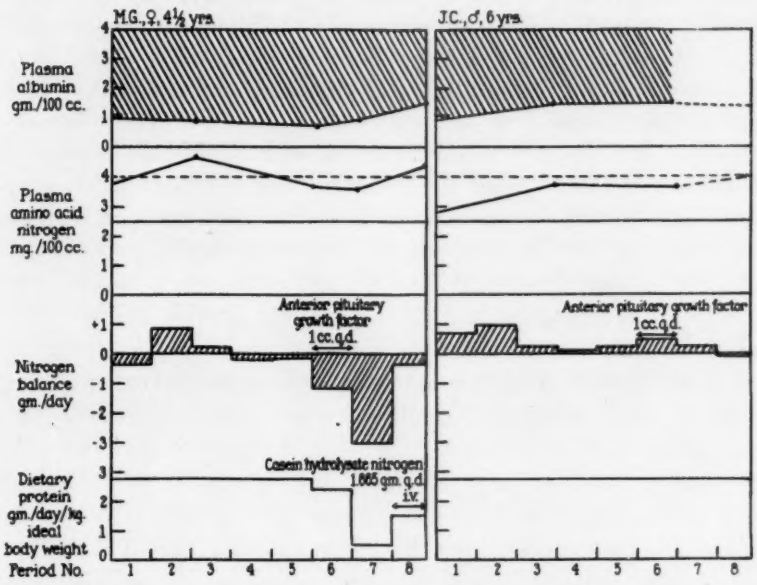
M.G., ♀, 4½ yrs.
J.C., ♂, 6 yrs.
Plasma albumin gm./100 cc.
Plasma amino acid nitrogen mg./100 cc.
Anterior pituitary growth factor 1 cc. q.d.
Nitrogen balance gm./day
Casein hydrolysate nitrogen 1.665 gm. q.d. i.v.
Dietary protein gm./day/kg. ideal body weight
Period No.

Chart 9.—Graphic representation of data from studies of nitrogen balance on M. G. and J. C. Note the plasma hypoaminoacidemia in J. C. and the fluctuating values for plasma amino acid nitrogen in M. G. The excessive nitrogen loss induced by the self-imposed fast was striking during period 7.

body weight. Another, J. C., was in positive nitrogen balance for the first seven of the eight periods, assimilating over the eight periods a daily average of 0.380 Gm. of nitrogen, or 0.023 Gm. per kilogram of ideal body weight. A third child, W. O'B., was in positive nitrogen balance during each of the periods except the first and the fifth. For the entire eight periods, including those in which a nitrogen loss occurred, this patient was in positive nitrogen balance, with an average assimilation of 0.136 Gm. of nitrogen per day, or 0.007 Gm. per kilogram of ideal body weight. The fourth child in this group, M. G., began her

hunger strike during the sixth period. For the first five periods her daily average assimilation of nitrogen was 0.086 Gm., or 0.006 Gm. per kilogram of ideal body weight.

The caloric intakes of these 4 children in excess of their requirements for basal metabolism as calculated in relation to estimation of surface area, according to the data of Lewis, Kinsman and Iliff [8] for normal children, were 39 per cent for W. O'B., 52 per cent for M. G. (for five weeks), 58 per cent for J. C. and 65 per cent for R. Q. The caloric excess over requirements for basal metabolism for J. C. in the earlier studies [9] was greater than that for R. Q. in this study. The 2 children, R. Q. and J. C., receiving the greatest caloric excess retained the most nitrogen. The differences in caloric intake between J. C. and M. G. were not significant. For all 6 children there was no apparent correlation between the caloric intake in relation to requirements for basal metabolism and the assimilation of nitrogen. It appears that in the group of children observed in several different studies from this clinic the development of "toxic" nitrogen metabolism [3] was of greater significance for nitrogen balance than the intake of a plethora of calories, and in this condition the excessive catabolism of nitrogen could not be significantly reduced by excessive caloric intake. It of course remains axiomatic that the diet should provide at least for the requirements for basal metabolism plus an increment to allow for activity, since a caloric deficit will be made up by equivalent destruction of tissue.

On the other hand, the 2 children fed the lower amounts of protein, about 2 Gm. per kilogram of ideal body weight per day, were both consistently wasting body nitrogen. In the eight weeks of study S. W. lost a daily average of 0.569 Gm. of nitrogen, or 0.048 Gm. per kilogram of ideal body weight per day. For the same period G. B. lost a daily average of 0.387 Gm. of nitrogen, or 0.026 Gm. per kilogram of ideal body weight per day. S. W.'s caloric intake was 59.3 calories per kilogram of ideal body weight per day, while G. B. received only 40 calories per kilogram. Again it would appear that nitrogen wasting in these 2 patients was affected slightly, if at all, by the variation in caloric intake, even when the caloric intake was below the expected basal requirements.

The fast undergone by M. G. deserves special comment. This child took her diet satisfactorily for five complete periods and through six

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8. Lewis, R. C.; Kinsman, G. M., and Iliff, I.: Basal Metabolism of Normal Boys and Girls from Two to Twelve Years Old, Inclusive, Am. J. Dis. Child. **53**: 348 (Jan., pt. 2) 1937.

9. Farr, L. E.: (*a*) Assimilation of Protein by Young Children with the Nephrotic Syndrome: Effect of Nephrotic Crises on Assimilation of Nitrogen, Am. J. Dis. Child. **58**:939 (Nov.) 1939; (*b*) II. Effect of Dietary Fat and Carbohydrate on Nitrogen Balance, ibid. **58**:935 (Nov.) 1939.

days of the sixth period. Thereafter for two days she vigorously refused all food, but she did take water with great reluctance. The negativistic attitude toward food was simultaneously extended toward all activities and steadfastly persisted despite the fact that Christmas was but three weeks off. It is significant that her nitrogen balance was negative for two weeks prior to the beginning of her fast. It appears likely that a somewhat greater loss of nitrogen prevailed during the first six days of period 6 than during the two preceding periods, since it is unlikely that a one day fast would increase the average nitrogen loss from 0.150 to 1.648 Gm. per day. Period 7 was a week of fasting during which no nitrogen was given parenterally. For this week her average daily intake was 1.234 Gm. of nitrogen, and her net nitrogen loss amounted to 3.021 Gm. per day, equivalent to 0.194 Gm. per kilogram of ideal body weight per day. During the first two days of period 8 the child took food providing but 42 calories. On the first day of this period infusions of dextrose and amino acids were begun. Over the two day period 700 cc. of amino acids was given in five infusions. On the third day an additional infusion of 100 cc. of amino acids was given. All infusions were 10 per cent solutions of amino acids. No further injections were given because the child began to eat satisfactorily a low calory, low protein diet. The nitrogen intake during period 8 averaged 4.372 Gm. per day, which was well below the expected minimal requirements for this child as shown by the first five periods. The increase in nitrogen intake over the preceding period amounted to an average of 3.138 Gm. per day, and of this 86 per cent was assimilated. It would appear possible that this unexpectedly high degree of assimilation may have been in this instance due at least in part to the intravenously administered amino acids.

The injection of 1 cc. of growth-promoting anterior pituitary extract had no apparent effect on the nitrogen balances. Intramuscular injections of this growth-promoting extract did, however, produce unexpected effects in the patients. Twenty-four to thirty-six hours after injection the site became exquisitely tender, coincident with the development of a smooth erythematous area on the skin centering about the point of needle puncture. In general appearance this erythematous area was strikingly similar to the erysipeloid reactions so frequently encountered in nephrotic children. In some instances the erythematous area extended from the elbow to the shoulder and halfway around the arm. During the latter part of the week injections were given in regions of the thigh. It was not uncommon for a previous site of injection to become erythematous and tender with subsequent injections, the reaction paralleling that at the site of the last injection. It must be emphasized that this reaction was elicited by the initial injections as well as by those following. During the week of injections the children became exceedingly pallid,

listless and irritable and began to lose their appetite. No sharp febrile reactions were seen, but low grade fever (temperatures up to 101 F.) was seen in S. W. and G. B. The similarity of the reactions in each of the 3 children was most striking.

Subsequently, this same growth-stimulating anterior pituitary extract was used repeatedly in treating a pituitary dwarf in the outpatient clinic, and no reactions of any sort were encountered. Injection of single doses into other types of patients elicited no cutaneous reactions and no untoward development of tenderness at the site of injection. When the injections of anterior pituitary extract were discontinued, the children regained their normal appearance, became cheerful and promptly recovered their appetites.

In 5 children the plasma amino acids were significantly below the normal level as described in earlier publications.[10] In 1, S. W., the concentration of amino acids in the plasma was within normal limits. There was no change in the level of the plasma amino acids during the period of therapy with anterior pituitary extract.

Significant changes in the level of the plasma albumin occurred only in M. G., and this was during the period of fasting, when nitrogen wasting and tissue destruction were at a maximum. As pointed out elsewhere,[3] the concentration of plasma protein may increase when the nephrotic patient is in negative nitrogen balance. Under these conditions any improvement in the level of plasma protein is temporary.

The ratio of urea plus ammonia nitrogen in the urine to total nonprotein nitrogen tended to remain constant in each child and was not influenced by the administration of pituitary extract.

COMMENT

The reports of Gaebler[11] and Lee and Schaffer[12] on the effect of anterior pituitary extracts showed that in animals under controlled conditions more nitrogen was assimilated when anterior pituitary extracts were given. Gaebler found that this assimilation was further increased when the animals had been in negative nitrogen balance. The doses used by these authors in their experiments were far greater than those used in this study. It is possible that failure to obtain this result in my patients was due to inadequate dosage. In my patients larger doses were contraindicated because of the reactions described.

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10. Farr, L. E., and MacFadyen, D. A.: Hypoaminoacidemia in Children with Nephrotic Crises, Am. J. Dis. Child. **59**:882 (April) 1940. Farr.[3]

11. Gaebler, O. H.: Some Effects of Anterior Pituitary Extracts on Nitrogen Metabolism Water Balance and Energy Metabolism, J. Exper. Med. **57**:349 (March) 1933.

12. Lee, M. O., and Schaffer, N. K.: Anterior Pituitary Growth Hormone and the Composition of Growth, J. Nutrition **7**:337 (March) 1934.

These reactions have also been seen in my patients when anterior pituitary extract derived from another animal species was used. No manifestations of allergic reaction to protein in the diet of a type similar to the proteins of the extract have been noted. Since, all told, 6 children with the nephrotic syndrome showed the same reaction to anterior pituitary extracts derived from two different animal species, it appears possible, but unlikely, that the reaction in some way involves the hormonal factors present and is not conditioned by the associated foreign protein. This type of reaction was not seen in a group of 12 nephrotic patients who received subcutaneous and intramuscular injections of commercial pitressin. Since the material eliciting a reaction in nephrotic children failed to cause visible reactions in other children, there exists a possibility that sensitivity to anterior pituitary extracts may be characteristic of this syndrome in children. On the other hand, Farr and Alpert [4] observed severe reactions in dogs to large doses of this same anterior pituitary extract given intravenously. Similar administration to the dogs of a variety of other endocrine extracts, including those containing other anterior pituitary fractions, caused no or very minor reactions. Until a product which is incapable of causing reactions in animals when given in large doses can be tested in nephrotic patients the possibility will remain that the reactions seen in these patients were due to a lowered threshold of reactivity and were in no way related to the specific substance which was injected.

The negative nitrogen balances observed in S. W. and G. B. were expected. However, the smaller loss of nitrogen by G. B. was not expected, since her caloric intake was below the requirements expected for basal metabolism. The requirements of G. B. for basal metabolism were 50 calories per kilogram of ideal body weight, but her intake was only 40 calories per kilogram. The expected requirements of S. W. for basal metabolism were 55 calories per kilogram, and her intake was 59 calories per kilogram of ideal body weight. Unfortunately, because of feeding difficulties, it was not possible to increase the caloric intakes of these 2 patients. The negative nitrogen balances seen in these 2 patients were similar to the type described as "toxic" nitrogen metabolism in an earlier publication, since the normal child will grow on a ration of 2 Gm. of protein per kilogram of ideal body weight.[3] However, the significance of a negative nitrogen balance on the basis of a nitrogen intake of 2 Gm. per kilogram of ideal body weight may be quite different from that observed when the amount of dietary protein has been pushed above 2.75 Gm. per kilogram of ideal body weight. In the latter instance the development of a negative balance definitely indicates, under most circumstances, the development of "toxic" nitrogen metabolism, and the nitrogen loss cannot be prevented by further increases of nitrogen intake.

A nephrotic crisis in patients fed low nitrogen and caloric diets might be expected to have as a precursor a sudden increase in the already negative balance. Since in this series of studies I have not been fortunate enough to observe the nitrogen balance when a nephrotic crisis developed under conditions of low nitrogen and caloric intakes, any explanation proffered must remain merely a conjecture. However, it is reasonable to suppose that the existence of a negative nitrogen balance favors the development of conditions leading to nephrotic crises.

In previous studies of nitrogen exchange J. C. was given diets which furnished 2 and 3 Gm. of protein and 77.5 [9a] and 73 [9b] calories per kilogram of ideal body weight. He maintained himself in positive nitrogen balance for a six week period on a diet containing 3 Gm. of protein per kilogram of body weight and actually assimilated a daily average of 0.026 Gm. of nitrogen per kilogram. This compares favorably with the figure of 0.023 Gm. per kilogram of ideal body weight per day found in the present study. On the diet containing 2 Gm. of protein per kilogram the patient showed a negative nitrogen balance for ten of the sixteen weeks and over the entire period retained a daily net average of but 0.001 Gm. of nitrogen per kilogram of ideal body weight. This evidence of failure of adequate calories alone to have a sufficient nitrogen-sparing action in this patient to permit attainment of equilibrium on 2 Gm. of protein per kilogram parallels the lack of correlation between caloric intake and nitrogen assimilation seen in the present study. It appears that in these patients the controlling factor in producing nitrogen assimilation is a reduction in the severity of the "toxic" nitrogen metabolism, with a corresponding decrease in the minimal nitrogen requirements. In a previous study it was shown that 2 Gm. of protein and 62.5 calories per kilogram of ideal body weight are adequate to promote rapid nitrogen assimilation during recovery from the disease when "toxic" nitrogen metabolism has disappeared.[9a]

That appetite alone and apparent ability to handle ingested food without digestive disturbances are an unsafe guide to protein intake requirements was shown by the negative balances of the 2 children fed the low protein diets. From this one may conclude that under circumstances demanding low caloric intakes by these children the protein content of the diet should approximate 3 Gm. of protein per kilogram of ideal body weight. On the other hand, when the child's appetite is such that calories greatly in excess of the diet are requested in my experience no harmful effects accrue from feeding high caloric and high protein diets. These periods were always transient in these patients and did not necessarily herald recovery or demonstrable improvement from the disease. Further studies on this point are highly desirable.

SUMMARY

Six children aged 2½ to 7 years with the nephrotic syndrome were observed in a study of nitrogen balance for eight weeks.

Evidence was adduced from these and previous observations that to avoid negative nitrogen balances in young nephrotic children the daily ration must contain more than 2.5 Gm. of protein per kilogram of ideal body weight. The assimilation of nitrogen in these children was little affected by increases in the caloric intake.

The administration of a growth-promoting extract of the anterior lobe of the pituitary had no effect on the nitrogen assimilation of 3 nephrotic children. Intramuscular administration of this pituitary extract caused local reactions in nephrotic children which were not observed when the same extract was given to other types of patients.

Data are presented on the nitrogen balance of a nephrotic child who underwent a rigorous two week self-imposed fast. Amino acids given intravenously at this time were assimilated to a greater degree than expected.

RESPIRATION IN NEWBORN INFANTS

A. ROBERT BAUER, M.D.
DETROIT

This work was done at Woman's Hospital, Detroit, as part of a study intended to clarify the present confusing criteria of normality of the newborn infant's chest. It was felt that any intelligent appraisal of the abnormal must be preceded by a clear understanding of the normal. This paper is concerned chiefly with the mechanics of respiration

The physiology of respiration in the newborn baby has been studied thoroughly. The observations of the older writers are referred to in most pediatric textbooks. A review of the subject with personal observations, has been presented separately by Wiggers [1] and by Foote.[2] This work was the result of clinical inspection, anatomic measurements and consideration of the relative functions of the chest and diaphragm during inspiration and expiration as ascertained by superimposed photographs, and it was primarily concerned with the rate, type and relative volume of respirations as compared with observations in the adult. There seemed to be general agreement on most matters. The respiratory rate was found to be high and variable (45 to 50 respirations per minute). It was also noted that there was no pause between inspiration and expiration and that there was a slight difference in the length of the two phases. The belief was expressed that inspiration was due entirely to the action of the diaphragm—that the wall of the chest because of its shape, elasticity and lack of muscular development, was unable to take part actively in respiration. Its role was merely to act as a rigid cavity, to withstand the pull of the diaphragm in much the same way that the wall of a cylinder withstands the pull of the piston. In fact, this concept is so generally accepted that some take the view that atelectasis may result directly from the inability of the chest to do this satisfactorily because of general asthenia, as seen in the premature infant. Studies of the movements of the chest and abdomen were made by pneumographic

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From the Pediatric Department of Woman's Hospital.

The cost of this study was defrayed by the Mendohlson Fund.

Dr. David J. Levy suggested this work and assisted with advice and criticisms.

1. Wiggers, C. J., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 3, p. 694.

2. Foote, J. A., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 3, p. 835.

tracings, which again confirmed the view that respirations were purely abdominal. No mention was made of whether the tracings were taken simultaneously. Figures on tidal air volume and vital capacity were obtained by means of a finely balanced spirometer, using a mouth piece. This had the obvious disadvantage of disturbing the baby.

More recently, the problem was approached in another manner by three different groups of investigators, Thorpe and Murphy,[3] Shaw and Hopkins [4] and Denning and Washburn.[5] They measured the tidal air, vital capacity and minute volume of air by using the reversed principle of the Drinker respirator. This permitted making records while the baby was asleep and probably introduced no factors which would alter normal respiration. The results of these investigators agreed generally with those of the older writers in the matter of rate and variations. They were able to show much more detail in the types of breathing. It seemed that the most outstanding finding was in the matter of variations in both rate and type in different babies studied under identical conditions and in the same babies studied under identical conditions but at different times—outstanding because it would seem to preclude the possibility of defining any normal standard for rate, type, depth or minute volume of respirations in newborn babies.

I felt that it would be desirable to have a more definite picture of the relative functions of the diaphragm and chest wall in normal respiration, particularly since such understanding is pertinent to the safe employment of any mechanical means to increase respiratory function. I attempted to get permanent quantitative records of these functions by encircling the chest and abdomen with fine steel wires enclosed in delicate coil springs. The wires were attached to recording levers, which made tracings on a revolving kymograph. Unfortunately, the movements were all lost in friction and the connections of the apparatus, and I had to give up this method in favor of the more delicate pneumograph, thereby losing much of the quantitative value.

MATERIAL AND METHOD

The apparatus (fig. 1) consisted of two cloth-enclosed rubber tubes (cigaret drains) similar to the cuff of a sphygmomanometer, one encircling the abdomen just above the navel and the other the chest at the nipple line. Each was attached to a recording tambour by means of small rubber tubing. A third pen recorded

3. Thorpe, E. S., and Murphy, D. P.: Breathing Measurements on Normal New-Born Infants, J. Clin. Investigation **10**:545 (Aug.) 1931.

4. Shaw, A. B., and Hopkins, T. R.: The Respirations of Premature Infants, Am. J. Dis. Child. **42**:335 (Aug.) 1931.

5. Denning, J., and Washburn, A. H.: Respirations in Infancy, Am. J. Dis. Child. **49**:108 (Jan.) 1935; **51**:832 (April) 1936.

the time in second intervals. Because of mechanical difficulties, I was not able to place both tambours in an upright position. One had to be inverted in order to get all three tracings on one drum. This did not affect the final result except that it made reading more difficult, because the upward stroke of the chest (upper) pen indicated contraction whereas the upward stroke of the abdominal (lower) pen indicated expansion.

After the tubes were properly applied, the baby was placed in his crib, covered and allowed to go to sleep. The tubes were then gently inflated, and the recording was started. Incidentally, the amount of positive pressure in the tubes did not affect the quantitative results, even if it was allowed to fall to atmospheric pressure, provided there were no leaks in the system. Fortunately, most of the tracings were obtained while the babies were asleep, some soundly and some lightly. Of those who were awake, a few were quiet, 2 had hiccups, some were crying and others had restless jerkings.

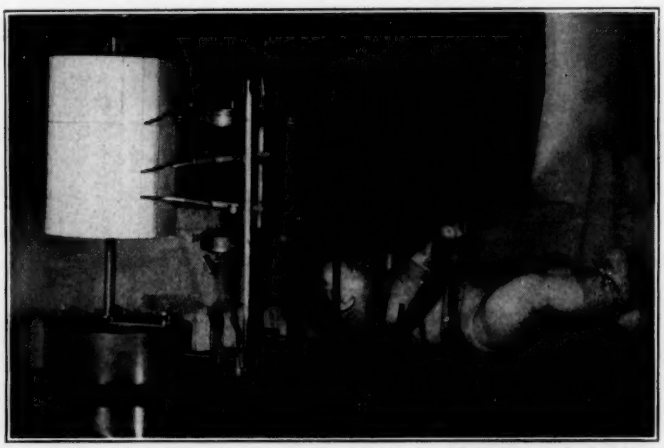

Fig. 1.—Arrangement of the apparatus. The undressed doll was placed on the table to show the application of the inflated "cuffs." During the actual test, the baby was fully clothed and covered in his crib. Note that the upper recording tambour is inverted to bring the tracings close together.

Nineteen infants were studied. The ages ranged from 1 to 10 days, the weights from 5 pounds 14 ounces (2,665 Gm.) to 8 pounds 14 ounces (4,026 Gm.). All were normal, healthy infants. The average time required for each test was about two hours. The actual tracings were made over a period of five to ten minutes, the rest of the time being spent adjusting the apparatus and getting the baby to sleep. In many instances I took the tracing two or even three times around the drum, elevating the drum slightly between revolutions. This gave much longer records, without disturbing the baby.

RESULTS

As the tracings were being made, it was noticed that the movements of the chest and the abdominal pen did not always have the same relation to each other. Most of the time the chest pen moved upward, slightly

in advance of the upward thrust of the abdominal pen. At other times they seemed to move simultaneously, but in opposite directions. At the time, I could not see anything in the baby's condition which was a possible cause of the change. However, later study of the records did throw some light on it.

The table summarizes the observations. The rates were higher and showed much more variation than those obtained by the older writers. The same degree of variation was present with reference to type. I was not able to show any typical pattern. Some followed the adult type, a sudden inspiratory effort followed by a slower, receding expiratory

Data of Nineteen Newborn Infants

Case No.	Sex	Age, Days	Weight, Lb. and Oz.	Respiratory Rate			Amplitude of Pen Movement, Mm.		Crying	Quiet	Comment
				Maximum	Minimum	Average	Abdomen	Chest			
1	M	5	7, 2	27	30	28	3	3	No	Yes	Bands too close
2	F	6	6, 10	90	105	97	1	1	No	Yes	
3	M	6	8, 14	54	60	57	2	1	No	Yes	
4	F	6	5, 14	36	60	48	9	1	Yes	No	
5	F	6	7, 5	60	78	69	2	1	No	Yes	
6	M	3	6, 8	48	84	66	3.5	1	No	Yes	
7	M	6	7, 10	120	120	120	20	7	Yes	No	Very irregular
8	M	10	6, 8	63	78	70	2	0.5	No	No	Apnea
9	F	5	8, 13	66	120	93	7	1	No	No	Hiccups
10	M	3	5, 15	24	105	66	5.5	0.5	No	Yes	
11	M	4	6, 15	51	57	54	11	5	Yes	No	Bands slipped
12	F	7	8, 9	39	54	46	5.5	2	No	No	Apnea
13	M	5	7, 8	66	123	94	6	1	No	Yes	
14	F	1	8, 6	48	72	60	3	0.5	No	Yes	
15	M	3	8, 3	48	90	69	3	1	No	Yes	
16	F	9	5, 15	..	..	46	..	..	No	Yes	
17	M	2	7, 1	..	..	34	..	..	No	Yes	
18	M	3	7, 2	78	120	89	3	1.5	No	Yes	
19	M	8	7, 2	30	68	49	4	1.25	No	Yes	

movement (see abdominal curve, fig. 2). Others showed a series of symmetric, undulating waves (see abdominal curve, fig. 3) usually considered more typical for a small baby. It will be noted that in the first instance the rate was slower and the amplitude greater than in the second.

It was this important observation that had escaped me while watching the movements of the pens. The importance lies in the fact that in the first instance the pens moved upward, indicating expansion of the abdomen with slight retraction of the chest, whereas in the second the pens moved in opposite directions, indicating that the chest and abdomen expanded together. Careful examination of figure 2 offers proof of this contention, for it will be seen that the base line of the chest curve—the line between respirations—is on the bottom. This means that the movement is an upward stroke, and since the tambour is inverted an

upward stroke necessarily indicates retraction of the wall of the chest. It will also be seen that this movement of the chest pen coincides with the upward stroke of the abdominal pen, which indicates expansion of the abdomen. Unfortunately, the same proof is not evident in figure 3. To establish the validity of this observation I tried several methods of

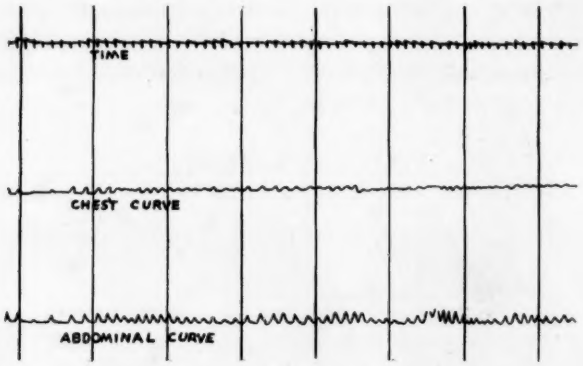

Fig. 2.—Part of the tracing from subject 19, showing retraction of the chest during inspiration.

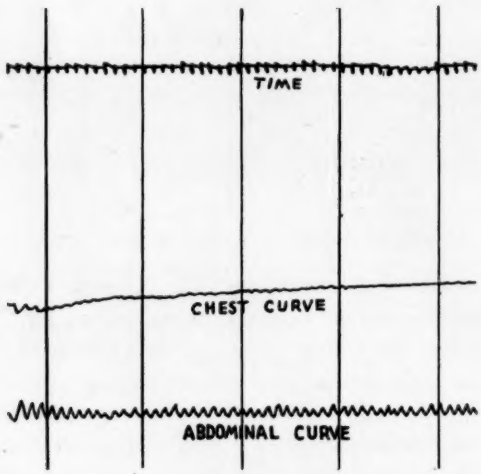

Fig. 3.—Another part of the tracing from subject 19, showing slight expansion of the chest during inspiration.

measuring and ruling the records and finally hit on the idea of taking moving pictures of the actual recordings. In projecting the film, I was able to stop it at any point, and the resulting "still" picture showed the exact relation of the pens to each other on their respective curves.

Figure 4 shows two such "still" pictures, one with both pens on the top of the curves and the other with one pen on the top and the other on the bottom. This again gives conclusive proof that the chest may either expand or contract with expansion of the abdomen.

Other data which I recorded, such as the occurrence of irregular breathing, apnea, hiccup, crying and stretching, have been considered

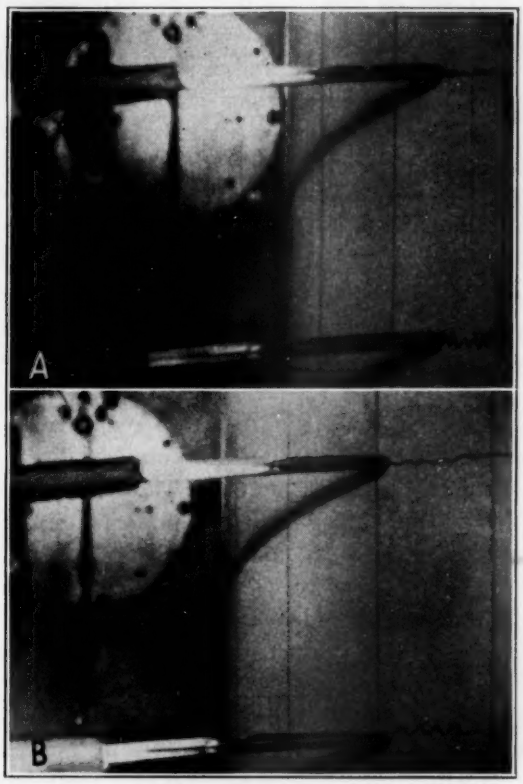

Fig. 4.—Enlargement of sections of the moving picture film, showing (*A*) both pens on the top of the curve, indicating retraction of the chest during inspiration and (*B*) one pen on the top of the curve with the other pen on the bottom of the curve, indicating that the chest expanded with expansion of the abdomen.

more thoroughly in other papers.[6] I merely call attention to the fact that hiccup, being an exaggerated diaphragmatic pull, resulted in a marked retraction of the chest wall. Crying, on the other hand, caused the most marked expansion of both chest and abdomen.

6. Thorpe and Murphy.[3] Shaw and Hopkins.[4] Denning and Washburn.[5]

COMMENT

An attempt was made to interpret these findings with a view to applying them practically. The most likely explanation was that in breathing the newborn infant attempts to follow the adult pattern of simultaneous expansion of the chest wall and descent of the diaphragm which result in inspiration. Because of the structure of the chest, its elasticity and relative muscular weakness, its expansion is so slight that it was barely recorded as a movement. This exposure occurred when respirations were rapid and shallow (see chest curve in fig. 3). However, when the respirations were slower and stronger, the wall of the chest was not able to withstand the more forceful pull of the diaphragm and the chest movement showed on the tracing as retraction rather than expansion (see chest curve, fig. 2). It is possible that other explanations may be offered. The one given seems the most logical, but two others were considered. The first was that the simultaneous expansion of chest and abdomen was the result of voluntary effort, the other type being a manifestation of involuntary breathing. This is not compatible with the actual curves shown in the photographs. The second, and more fanciful, assumed that the chest responded to every nerve impulse by expanding, but that because the nerve control of the muscles of the chest and that of the diaphragm were poorly coordinated, they worked together some times and in opposite directions at others. My general impressions, however, do not support this view.

From the practical point of view, these findings do not seem to contribute much to knowledge about the causation, diagnosis or treatment of disorders of respiration in the newborn except in a negative way. For instance, weakness of the wall of the chest has been considered a possible cause of atelectasis; yet it was found in some degree in most of the babies studied. This suggests that other causes are more likely, such as cohesion of the moist surfaces of the alveolar walls, as shown by Wilson and Farber,[7] obstruction of bronchi by mucous plugs, congenital malformation of bronchial or pulmonary structures or any other local condition which prevents the normal expansion of pulmonary tissue. Moreover, the fact that normal infants have such a high respiratory rate, with equally marked variations in type, tends to lessen the importance of this factor in diagnosis. From the standpoint of therapy, these same considerations argue against mechanical interference with the respiratory movement except when breathing has never started or when it has stopped completely, for, obviously, unless such apparatus as may be employed to carry on artificial respiration is timed perfectly, so as to supplement the baby's own efforts, it hampers these efforts without con-

7. Wilson, J., and Farber, S.: Pathogenesis of Atelectasis of the New-Born, Am. J. Dis. Child. **46**:590 (Sept.) 1933.

tributing any aid on its own account. A possible helpful adjunct to therapy suggested by this work is something in the nature of strapping or a vacuum which, applied to the chest alone, would hold it in continuous expansion. This would increase aeration slightly by eliminating the small amount of retraction which results from the more forceful pull of the diaphragm in labored breathing. So far, nothing practical of this type has been designed, although Wilson [8] has recently advocated a similar measure. He has expressed the belief that the Drinker respirator can be controlled manually so as to hold the chest and abdomen in a position of expansion for as long as a minute at a time in order to give some slight aid to feeble respiration. The effect from this maneuver would be somewhat the same as that from my suggestion and without interference with expiration by too long an application. However, until some mechanical aid of the type suggested is available, one must rely on the passive administration of oxygen or oxygen and carbon dioxide, such as was described in a previous communication,[9] in conjunction with the other accepted forms of therapy.

The matter of a "lusty cry" seems to deserve mention. As stated before, crying caused the greatest degree of expansion of both abdomen and chest observed on any of the records. In order to cry, a baby must first take a large breath, thereby expanding all of the pulmonary tissue which is capable of expansion, with the least danger of rupturing alveolar walls. Needless to say, this is probably the oldest and most widely used treatment for cyanotic babies who are not breathing properly, and if it is used intelligently, it probably has some merit in cases of simple atelectasis. However, some of the methods used to stimulate the baby to cry have been properly condemned because of the danger of further traumatizing an infant already suffering from intracranial hemorrhage. With this in mind, such stimulation should be gentle and not too frequent when hemorrhage is suspected or when response is negligible, as it must be remembered that asphyxiated babies are "profoundly depressed," as reiterated by Flagg.[10]

CONCLUSIONS

An attempt was made to get permanent, simultaneous quantitative records of the movements of the chest and abdomen in normal, healthy newborn infants by means of pneumographic tracings taken during sleep. Nineteen full term babies were studied. Their ages ranged from 1 to 10 days and their weights from 5 pounds 14 ounces to 8 pounds 14 ounces.

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8. Wilson, J.: Personal communication to the author, April 1940.

9. Bauer, A. R.: A Combination Resuscitator and Incubator for New-Born Infants, J. A. M. A. **108**:1874 (May 29) 1937.

10. Flagg, P. J.: Treatment of Asphyxia Neonatorum, J. Maine M. A. **31**:1 (Jan.) 1940.

The results showed extreme variations in respiratory rate, ranging from 24 to 120 per minute, with the average about 60. The amplitude of the abdominal movement was from two to five times as great as that of the chest. It was found that at times the chest expanded slightly with expansion of the abdomen, but that at other times there was a retraction of the chest just before full expansion of the abdomen. Both phases were present in all babies studied.

These observations were explained on the basis that when breathing was rapid and shallow the chest expanded with the abdomen, but that when breathing was slower and deeper the more forceful pull of the diaphragm produced retraction of the relatively weak elastic chest wall.

The findings offer nothing new to understanding of the causation. diagnosis or treatment of disorders of respiration in the newborn except to emphasize the need for caution against placing too much reliance on the rate, the type or the depth of respirations in explaining or treating neonatal asphyxia.

Case Reports

RICKETS ASSOCIATED WITH DWARFISM, GLYCOSURIA, KETONURIA AND ALBUMINURIA

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Since the presentation of a case of nephritis associated with rachitic changes in the long bones by Lucas [1] in 1883, the subject of renal rickets has been widely discussed in English and American literature. Its pathology and chemical physiology, as well as the various etiologic factors involved, have been carefully considered by Parsons,[2] Mitchell,[3] Schoenthal and Burpee,[4] Hamperl and Wallis,[5] Shelling and Remsen [6] and others. In brief, this disturbance is characterized by chronic renal disease, dwarfism, hyperphosphatemia, azotemia, changes in the skeleton simulating those in infantile rickets, chronic acidosis and, finally, uremia and death.

Of late, several cases have been reported in which the clinical and roentgenologic findings simulated those of renal rickets, except for the absence of azotemia and the presence of hypophosphatemia instead of the usual hyperphosphatemia. De Toni [7] presented an unusual case

From the Department of Pediatrics of the Jewish Hospital.

1. Lucas, R. C.: Form of Late Rickets Associated with Albuminuria, Lancet **1**:993, 1883.

2. Parsons, L.: Infantilism Associated with Chronic Interstitial Nephritis, Brit. M. J. **2**:481, 1911; Bone Changes in Renal and Coeliac Infantilism, Arch. Dis. Childhood **2**: 1 and 198, 1927.

3. Mitchell, A. G.: Nephrosclerosis (Chronic Interstitial Nephritis) in Childhood with Special Reference to Renal Rickets, Am. J. Dis. Child. **40**:101 (July); 345 (Aug.) 1930; A Note on the Pathogenesis of Renal Rickets, J. Pediat. **3**:192, 1933.

4. Schoenthal, L., and Burpee, C.: Renal Rickets, Am. J. Dis. Child. **39**:517 (March) 1930.

5. Hamperl, H., and Wallis, K.: Ueber renalen Zwergwuchs ohne und mit (renaler) Rachitis, Ergebn. d. inn. Med. u. Kinderh. **45**:589, 1933; Ueber "renale Rachitis" und "renale Zwergwuchs," Virchows Arch. f. path. Anat. **288**:119, 1933.

6. Shelling, D., and Remsen, D.: Renal Rickets, Bull. Johns Hopkins Hosp. **47**:158, 1935.

7. de Toni, G.: Remarks on Relation Between Renal Dwarfism and Renal Diabetes, Acta pædiat. **16**:479, 1933.

of rickets associated with albuminuria, glycosuria, hypophosphatemia and dwarfism but with no nitrogen retention. In this instance, there was a history of consanguinity, the father and mother being first cousins. Fanconi [8] reported the cases of 3 dwarfed girls, all under 4 years of age, who, like de Toni's patient, presented rachitic changes in the long bones, albuminuria, glycosuria, hypophosphatemia and a normal concentration of nonprotein nitrogen in the blood. A familial tendency was noted in 1 instance and consanguinity in another. Two of the patients succumbed to the disease, and their tissues were examined histologically. The long bones showed lesions similar to those observed in infantile rickets. The renal tubules showed only slight degenerative changes in 1 case but much more advanced changes in the other. The liver in 1 case showed fatty degeneration. The glomeruli of the kidneys presented no pathologic alterations in either case.

In 1937, Guild and her associates [9] reported, before the Society for Pediatric Research, an instance of severe rickets occurring in a 10 month old girl who also showed glycosuria, albuminuria, hypophosphatemia and chronic acidosis. The child was observed for many months, during which time she gained neither in height nor in weight.

The clinical and laboratory findings in the case to be described, although closely resembling those observed by de Toni, Fanconi and Guild and her associates, differ sufficiently from their descriptions to warrant recording.

REPORT OF A CASE

E. S., a 5 year old girl of Jewish parentage, was first seen in the pediatric outpatient department at 2 years of age, at which time the chief complaints were (1) poor appetite and (2) frequent colds. She was born at term and weighed 8 pounds 2 ounces (3,685 Gm.). Delivery was normal and spontaneous, and there were no untoward postpartum incidents. She was breast fed for four months and was given orange juice and cod liver oil from the age of 6 weeks. She weighed 20 pounds (9 Kg.) at the end of one year. She walked before she was 1 year old, but owing to a severe attack of pertussis at the age of 1 year, which confined her to bed for a long time, she did not resume walking until she was 16 months of age. Her second year of life was uneventful, except that she had frequent colds and suffered from periods of anorexia. The only positive fact elicited from the family history was that the patient's sister had died at the age of 10 months, presumably of rickets and pneumonia. There was no consanguinity in the family. Physical examination at the end of her second year showed no skeletal deformities. Her fontanels were closed, and her gait was normal. Her heart and lungs were normal to percussion and auscultation. The edge of the liver was felt about 1½ fingerbreadths below the costal margin. The diagnosis at that time was acute tonsillitis.

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8. Fanconi, G.: Der frühinfantile nephrotisch-glykosurische Zwergwuchs mit hypophosphatämischer Rachitis, Jahrb. f. Kinderh. **147**:299, 1936.

9. Guild, H. G.; Pierce, J. A., and Lilienthal, J. L., Jr.: An Unfamiliar Rachitic Syndrome, Am. J. Dis. Child. **54**:1186 (Nov.) 1937.

The patient did not return to the outpatient clinic until nearly two and one-half years later, that is, until she was almost 4½ years of age. The child was apparently well until the age of 3½ years, at which time her mother noticed that she was unsteady of gait and fell frequently. She continually sought support while walking and finally refused to walk at all. She had attended several clinics, where she was treated with large doses of vitamin D apparently without curing the rickets. She was admitted to the hospital for study.

The findings on admission to the hospital were as follows: She appeared small for her age, weighing only 31 pounds (14 Kg.) and measuring 37½ inches (94 cm.) in height. The circumference of the head measured 19 inches (48 cm.). The epiphyses of both upper and lower extremities were enlarged, and the ribs flared outward, the latter deformity accentuating the pot belly. The fontanels were closed, and there were no signs of craniotabes. The gait was waddling, and the posture was that of genu valgum. The heart and lungs were normal. The liver was palpable 1½ fingerbreadths below the costal margin, and the spleen was felt just at the costal margin. The urine was acid in reaction, and its specific gravity varied from 1.012 to 1.028. It contained albumin in quantities varying from a trace to 2 plus and sugar in amounts up to 0.4 per cent. The urine also contained granular and hyaline casts and varying amounts of acetone. The blood pressure varied from 110 to 115 systolic and from 70 to 90 diastolic. Roentgenograms of the long bones revealed marked fraying of the epiphyses, broadening of the diaphysial ends of the bones and marked osteoporosis of the shafts (fig. 1). The concentration of serum calcium was 10.8 mg., of inorganic phosphorus 2 mg., of cholesterol 276 mg. and of chlorides 375 mg. per hundred cubic centimeters. The carbon dioxide–combining power of the blood was 36 volumes per cent, and the amount of serum phosphatase was 32 units (Bodansky). The hemoglobin content was 90 per cent; erythrocytes numbered 4,700,000 and leukocytes 12,000, with a normal differential count. A stained blood film failed to reveal any pathologic white or red cells. The reducing substance in the urine was found to consist of dextrose and fructose in nearly equal proportions. An intramuscular injection of phenolsulfonphthalein showed an excretion of 79 per cent in the urine in two hours, while an intravenous injection yielded an excretion of 65 per cent. Tuberculin reactions were negative in all dilutions, and the Wassermann and Kline reactions were likewise negative.

In view of the history that the rickets had progressed in spite of apparently adequate vitamin D therapy, a metabolic study was undertaken to determine whether or not the rickets was of the ordinary infantile type and whether it was totally or only partially refractory to vitamin D therapy. The child was placed on a diet consisting of a powdered whole milk mixture, cream (40 per cent), orange and prune juices and cane sugar. Samples of the diet were analyzed for calcium, phosphorus, potassium, magnesium, chloride, sodium and nitrogen. The diet yielded 60 calories per kilogram of body weight per day and a calcium: phosphorus ratio of 1.4: 1. The patient was on this diet for a week before the metabolic studies were started. With the exception of four periods of study which lasted five or six days, all metabolic periods were of three days' duration. The daily intake was measured accurately, and the urine and feces were collected each day. The accuracy of the collections of urine was checked by determining the excretion of creatinine in daily specimens. For the collection of feces, the beginning and end of each period was marked off by the oral administration of carmine. At the beginning of the metabolic studies, the blood serum was analyzed for calcium, phosphorus, carbon dioxide, magnesium, nonprotein nitrogen, total nitrogen, cholesterol, chlorides, total base and phosphatase. At the beginning and end of the various subsequent

periods, the concentrations of calcium and phosphorus in the serum were followed more closely. The total base, nonprotein nitrogen, total nitrogen, phosphatase, carbon dioxide–combining power, total lipids, lipid phosphate and ketone bodies were also determined on several occasions (table 1).

After the first control period, 25 drops of crystalline vitamin D in propylene glycol[9a] (6,250 U. S. P. units of vitamin D) was added daily to the diet, and the child was allowed a "free period" of three days before the second experimental period was started.

In order to observe the gradual changes in the mineral metabolism that might occur if healing of the rachitic process was induced, the subsequent fifteen days were divided into five periods of three days each. At the end of the last period of administration of vitamin D, the level of inorganic phosphorus in the blood was found to be no higher than at the beginning of the experiment, namely, 2 mg.

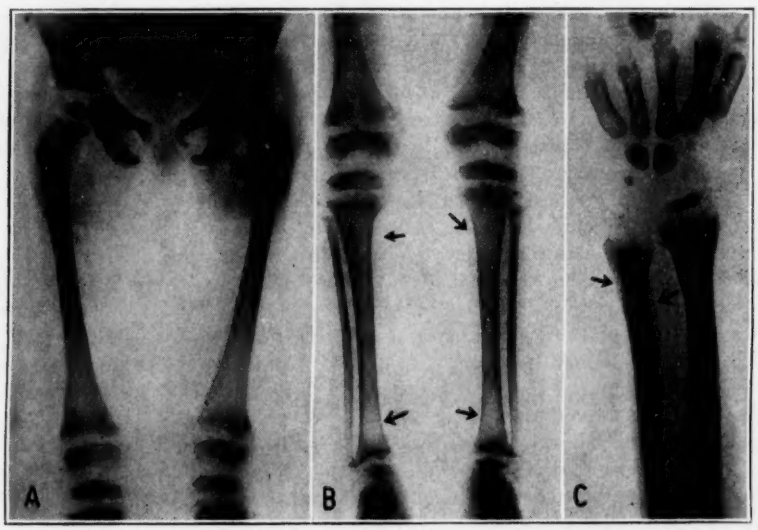

Fig. 1.—Roentgenograms taken three months before metabolic studies were begun. *A* shows shortening of the neck of both femurs, marked osteoporosis, fraying at both ends of both femurs and upper ends of the tibias and irregular areas of calcification in the metaphyses at the knee. *B* shows the rachitic changes in the bones at the knees and ankles. Growth lines (indicated by arrows) are visible at the upper and lower ends of the tibias. *C* shows marked cupping of the epiphyses and widening and irregular calcification of the metaphyses of the radius and ulna. The centers of ossification are indistinct, irregular and small. There is also a periosteal reaction (indicated by arrows) at the distal end of the ulna.

per hundred cubic centimeters. Accordingly, it was decided to attempt to increase the inorganic phosphorus in the blood by adding inorganic phosphorus to the diet in the form of phosphoric acid (H_3PO_4). The daily dose was 15 cc. of a 10 per cent solution, administered in fruit juice. After initiating this therapy a period of five days was allowed to elapse before another series of experiments, which lasted

9a. The preparation used was drisdol.

TABLE 1.—*Chemical Constituents of the Blood in a Case of Rickets Associated with Dwarfism, Glycosuria, Ketonuria and Albuminuria*

Date	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Sodium, Mg. per 100 Cc.	Potassium, Mg. per 100 Cc.	Magnesium, Mg. per 100 Cc.	Chloride, Mg. per 100 Cc.	Total Base, mEq.	Carbon Dioxide, Volumes per Cent	Total Protein, Gm. per 100 Cc.	Albumin, Gm. per 100 Cc.	Globulin, Gm. per 100 Cc.	Non-protein Nitrogen, Mg. per 100 Cc.	Urea Nitrogen, Mg. per 100 Cc.	Total Lipids, Mg. per 100 Cc.	Lipid Phosphate, Mg. per 100 Cc.	Cholesterol, Mg. per 100 Cc.	Phosphate,* Mg. per 100 Cc.	Acetone Bodies Mg. per 100 Cc.
3/ 6/36.....	11.4	2.3	...	....	...	...	...	....	....	...	...	....	....	....	...	...	33.7	...
4/20/36.....	10.8	2.0	...	....	...	375	...	36	7.5	5.6	1.9	23.0	....	....	...	276	32.0	...
5/28/36.....	11.5	2.1	...	....	...	374	...	36	7.47	...	...	24.0	....	....	...	354	....	...
6/ 2/36.....	9.95	1.8	...	....	1.3	387	146	44	....	...	...	....	....	....	...	...	....	...
6/ 9/36.....	10.7	1.8	...	....	1.45	...	...	53.5	....	...	...	....	....	....	...	...	....	...
6/13/36.....	10.3	2.0	...	....	...	...	...	....	....	...	...	....	....	....	...	...	....	...
6/18/36.....	10.6	2.1	...	....	...	...	...	....	....	...	...	....	....	....	...	...	....	...
6/24/36.....	....	2.0	...	....	...	...	...	....	....	...	...	....	....	....	...	...	....	...
7/ 2/36.....	10.5	2.6	...	....	...	...	...	48.7	....	...	...	....	....	....	...	...	....	...
7/15/36.....	10.7	1.5	...	....	...	350	...	44.6	6.17	...	...	34	....	....	...	350	....	...
7/30/36.....	11.2	1.8	...	....	...	372	155	....	....	...	...	....	....	....	...	...	....	...
8/16/36.....	10.5	3.3	...	....	...	...	...	....	....	...	...	....	....	....	...	...	....	...
9/ 1/36.....	9.2	2.4	...	....	2.4	...	...	....	....	...	...	....	....	....	...	...	....	...
9/ 3/36.....	10.1	2.1	...	....	...	...	...	....	....	...	...	....	....	....	...	...	....	...
10/19/36.....	9.7	1.7	...	....	3.2	...	...	....	....	...	...	....	....	....	...	...	....	...
11/27/36.....	9.5	1.9	...	....	2.1	...	...	....	6.1	...	...	16	....	....	...	190	27.9	...
4/16/37.....	10.5	2.3	...	....	...	...	...	....	....	...	...	....	....	....	...	...	34.1	...
5/20/37.....	9.6	2.3	...	....	...	...	...	....	....	...	...	....	....	....	...	...	23.8	...
7/15/37.....	11.0	2.3	305	....	1.8	350	151	28	6.87	...	...	....	....	....	...	205	22.7	...
8/10/37.....	....	2.6	...	....	...	...	...	....	....	...	...	....	....	896	8.0	171	....	11.3
10/ 6/37.....	....	2.2	...	....	...	...	...	33	....	...	...	....	....	....	...	...	....	9.0
1/24/38.....	10.1	2.1	...	....	2.4	...	...	39	....	...	...	18	....	507	5.2	223	21.9	...
8/18/38.....	12.2	1.8	...	12.6	...	370	145	....	7.07	...	...	21	....	607	7.2	162	29.8	...
10/27/38.....	10.2	2.1	...	13.5	...	...	...	42.7	....	...	...	....	11.8	....	...	186	30.9	...
3/20/39.....	10.7	3.1	333	16.7	2.0	...	148	42.3	....	...	...	23.7	19.2	649	6.4	237	23.6	...

* Bodansky units.

two weeks, was started. At the end of this period the inorganic phosphorus of the blood still remained low, in spite of the addition of phosphate to the diet.

The special diet and the vitamin D were discontinued for two weeks, and the child was allowed to partake of the regular ward diet. The special diet was then resumed, and another control period was obtained. After this period, she was again permitted to eat the ward diet without the addition of vitamin D for a period of ten weeks. Then she was again placed on the experimental diet, to which was added calcium phosphate ($CaHPO_4.2H_2O$). She remained on this diet for several days, and then her mineral metabolism was observed for a three day period. Then vitamin D, in addition to calcium phosphate ($CaHPO_4.2H_2O$), was introduced and the mineral balance studied for another period. The results of these studies are shown in figure 2 and table 2.

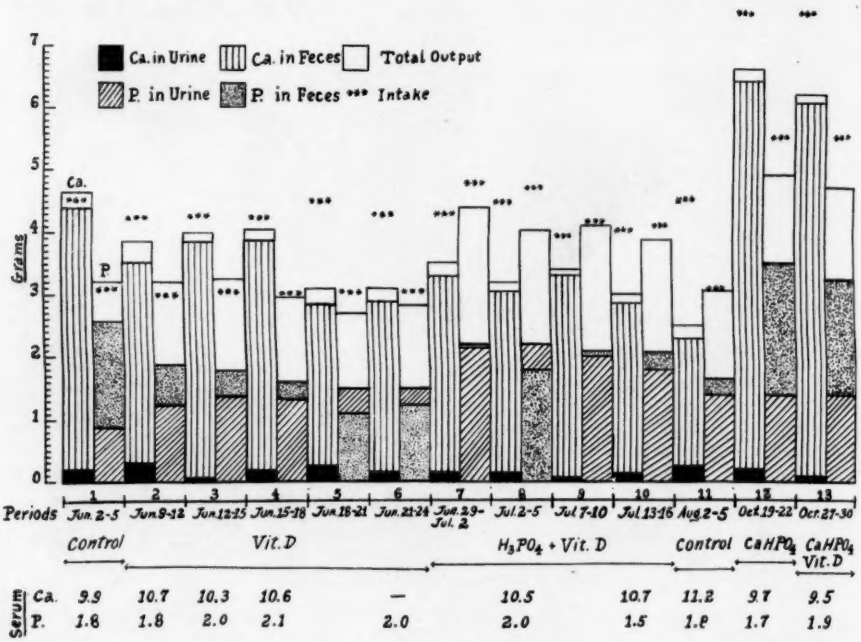

Fig. 2.—Comparison of intake and output of calcium and phosphorus during thirteen periods of observation.

The metabolic studies revealed that she was in negative calcium balance in the first control period and that she was in positive balance immediately after the administration of vitamin D. The phosphorus balance, however, remained negative up to the fourth period, after which time she retained both calcium and phosphorus. The retention of both these elements continued in the subsequent periods, irrespective of the therapeutic agents employed.

The ratio of calcium retained to phosphorus retained in cases of ordinary healing rickets is said to be 2:1 (Orr, Holt and associates[10]). However, this ratio was obtained in our patient only when both phosphoric acid and vitamin D were admin-

10. Orr, W. J.; Holt, L. E., Jr.; Wilkins, L., and Boone, F. H.: Calcium and Phosphorus Metabolism in Rickets, with Special Reference to Ultraviolet Ray Therapy, Am. J. Dis. Child. **26**:362 (Oct.) 1923.

istered. During all other periods of administration of vitamin D the ratio fluctuated from 4:1 to 7:1. When the phosphoric acid and vitamin D were discontinued for a period of two weeks, the ratio of calcium retained to phosphorus retained fell to 47:1, that is, to an almost negative phosphorus balance. When calcium phosphate was added to the diet, with or without vitamin D, the ratio of calcium retained to phosphorus retained returned to 2:1.

The calcium and phosphorus ratio of 2:1 corresponds to that found in bones and would seem to indicate that calcium phosphate was being deposited in the bones, but on closer analysis of the actual amounts retained per day per kilogram of body weight (table 2), it becomes evident that the retention was small. Indeed, it was no more than is often seen in patients with active infantile rickets before vitamin D therapy is instituted.

In addition to the calcium and phosphorus studies, the metabolism of the other mineral elements and of nitrogen was also investigated in all the experimental periods. The nitrogen metabolism was studied with the hope of finding some explanation for the slow gain in weight and the mineral balance was investigated because of recent studies which indicate that the metabolism of minerals other than calcium and phosphorus may be involved in diseases of the osseous system. Albright and Ellsworth [11] and Shelling and his associates [12] found that parathyroid extract produces a loss not only of calcium and phosphorus but also of sodium and chloride, and Bassett and Van Alstine [13] noted a positive balance of these elements, as well as of calcium and phosphorus, in patients subjected to parathyroidectomy for osteitis fibrosa. Heyman [14] studied the mineral metabolism in cases of ordinary rickets and found it to be within normal limits; but since the rachitic process in our patient appeared to be unusual, it was hoped that such a study would shed some light on the disturbance in lime salt metabolism, analogous to that found in parathyroid dysfunction.

The results of these studies are shown in table 2 and figure 2. The nitrogen, sodium and chloride balances were positive throughout all the experimental periods, with the exception of the second, when vitamin D was first administered. The magnesium balance was positive in all periods; and the potassium balance was positive in all the periods until calcium phosphate was administered, when it became negative. The potassium balance improved somewhat when vitamin D was added to the diet, but still remained negative. The reason for the negative potassium balance during the periods of administration of calcium phosphate is not clear, especially in the presence of a positive nitrogen balance. The negative nitrogen balance during the first period of feeding vitamin D may be explained on the basis of suddenly increased catabolism, since Reed and his associates [15] have shown that this vitamin increases the metabolic rate in experimental animals.

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11. Albright, F., and Ellsworth, R.: Calcium and Phosphorus Studies in a Case of Idiopathic Hypoparathyroidism, J. Clin. Investigation **7**:183, 1929.

12. Shelling, D. H.; Kadji, L., and Guth, L., in Shelling,[27] p. 98.

13. Bassett, S. H., and Van Alstine, H. E.: Mineral Exchanges of Man: The Effect of Extirpation of Parathyroid Tumor on the Balance of Electrolytes, J. Nutrition **9**:345, 1935.

14. Heyman, W.: Nitrogen, Potassium, Sodium and Chloride Metabolism in Rickets, J. Exper. Med. **64**:471, 1936.

15. Reed, C. I.: Effect of Heavy Administration of Viosterol on the Metabolism of the Rat, Proc. Soc. Exper. Biol. & Med. **32**:274, 1934. Reed, C. I.; Thacker, E. A.; Dillman, L. M., and Welch, J. W.: The Effects of Irradiated Ergosterol on the Metabolism of Normal Dogs, J. Nutrition **6**:355, 1933.

Because the patient showed persistent glycosuria, dextrose tolerance tests were made on several occasions (fig. 3). The blood sugar curves obtained revealed that during fasting the patient tended to be hypoglycemic and that the curves

TABLE 2.—*Data from Studies of Mineral*

	Ca, Gm.	P, Gm.	K, Gm.	Na, Gm.	Mg, Gm.	Cl, Gm.	N_2, Gm.	Comment
Period 1: Control								
Excretion:								
Urine	0.208	0.890	4.290	0.945	0.045	3.398	13.033	Weight: 13.4 Kg.
Stool	4.403	2.317	0.184	0.019	0.619	0	2.424	Duration of
Total	4.611	3.207	4.474	0.964	0.664	3.398	15.457	period: 6/2-6/5
Intake	4.525	3.133	6.929	1.757	0.671	3.869	14.407	
Balance	—0.086	—0.074	2.455	0.793	0.007	0.471	1.050	
Balance/d/k	—0.002	—0.002	0.061	0.020	0.000	0.012	0.026	
Period 2: 25 Drops Daily of Crystalline Vitamin D in Propylene Glycol								
Excretion:								
Urine	0.310	1.315	2.293	1.771	0.066	4.634	14.732	Weight: 13.4 Kg.
Stool	3.549	1.888	0.487	0.016	0.512	—	1.599	Duration of
Total	3.859	3.203	2.780	1.787	0.578	4.634	16.331	period: 6/9-6/12
Intake	4.272	2.981	6.752	1.663	0.639	3.923	15.457	
Balance	0.413	—0.222	3.972	—0.124	0.061	—0.711	—0.864	
Balance/d/k	0.010	—0.005	0.098	—0.003	0.002	—0.018	—0.021	
Period 3: 25 Drops Daily of Crystalline Vitamin D in Propylene Glycol								
Excretion:								
Urine	0.090	1.429	4.687	1.392	0.019	3.276	13.295	Weight: 13.4 Kg.
Stool	3.870	1.794	1.230	0.028	0.516	—	1.542	Duration of
Total	3.960	3.223	5.917	1.420	0.535	3.276	14.837	period: 6/12-6/15
Intake	4.302	3.043	7.063	1.686	0.654	4.199	15.065	
Balance	0.342	—0.180	1.146	0.266	0.119	0.923	0.228	
Balance/d/k	0.008	—0.004	0.028	0.006	0.003	0.022	0.006	
Period 4: 25 Drops Daily of Crystalline Vitamin D in Propylene Glycol								
Excretion:								
Urine	0.191	1.349	2.517	1.195	0.030	2.850	11.130	Weight: 13.4 Kg.
Stool	3.870	1.611	0.369	0.069	0.533	—	1.847	Duration of
Total	4.061	2.960	2.886	1.264	0.563	2.850	12.977	period: 6/15-6/18
Intake	4.250	2.910	6.379	1.637	0.622	3.655	14.372	
Balance	0.189	—0.050	3.493	0.373	0.059	0.805	1.395	
Balance/d/k	0.005	—0.001	0.087	0.009	0.002	0.020	0.034	
Period 5: 25 Drops Daily of Crystalline Vitamin D in Propylene Glycol								
Excretion:								
Urine	0.242	1.493	4.208	1.494	0.071	3.408	11.922	Weight: 13.4 Kg.
Stool	2.849	1.193	0.469	0.077	0.311	—	1.560	Duration of
Total	3.091	2.686	4.677	1.571	0.382	3.408	13,482	period: 6/19-6/22
Intake	4.508	3.016	6.781	1.769	0.664	3.875	15.332	
Balance	1.417	0.330	2.104	0.198	0.282	0.467	1.850	
Balance/d/k	0.035	0.008	0.052	0.005	0.007	0.011	0.046	
Period 6..: 25 Drops Daily of Crystalline Vitamin D in Propylene Glycol								
Excretion:								
Urine	0.189	1.519	3.573	1.219	0.076	2.976	13.383	Weight: 13.4 Kg.
Stool	2.899	1.316	0.239	0.016	0.332	—	1.044	Duration of
Total	3.088	2.835	3.812	1.235	0.408	2.976	14.427	period: 6/22-6/25
Intake	4.297	3.011	6.930	1.671	0.646	3.158	14.872	
Balance	1.109	0.176	3.118	0.436	0.238	0.182	0.445	
Balance/d/k	0.028	0.004	0.078	0.011	0.006	0.004	0.011	
Period 7: 25 Drops Daily of Crystalline Vitamin D in Propylene Glycol Plus 15 Cc. of a 10 per Cent Solution of H_3PO_4								
Excretion:								
Urine	0.161	2.172	2.720	1.178	0.084	2.848	12.992	Weight: 13.8 Kg.
Stool	3.296	2.200	0.345	0.041	0.405	—	1.247	Duration of
Total	3.451	4.372	3.065	1.219	0.489	2.848	14.289	period: 6/29-7/2
Intake	4.277	4.768	6.626	1.665	0.635	3.174	14.737	
Balance	0.820	0.396	3.561	0.446	0.146	0.326	0.498	
Balance/d/k	0.019	0.010	0.086	0.011	0.003	0.007	0.011	

exhibited a general tendency toward a sustained level. These observations led to a study of her respiratory quotient The total respiratory quotients were determined by indirect colorimetry, Bailey's method[16] being used. The first

16. Bailey, C. V.: Apparatus Used in the Estimation of Basal Metabolism, J. Lab. & Clin. Med. **6**:657, 1921.

respiratory quotient on fasting was 0.75. Twenty-five grams of dextrose was administered orally, and after one and a half hours the respiratory quotient was 0.76. Several months later this determination was repeated. On fasting the

Metabolism During Thirteen Periods of Observation

	Ca, Gm.	P, Gm.	K, Gm.	Na, Gm.	Mg, Gm.	Cl, Gm.	N_2, Gm.	Comment
Period 8: 25 Drops Daily of Crystalline Vitamin D in Propylene Glycol Plus 15 Cc. of a 10 per Cent Solution of H_3PO_4								
Excretion:								
Urine	0.156	2.211	3.348	1.242	0.084	2.940	12.453	Weight: 13.6 Kg.
Stool	3.045	1.833	0.240	0.070	0.360	—	0.930	Duration of
Total	3.201	4.044	3.588	1.312	0.444	2.940	13.383	period: 7/2-7/5
Intake	4.518	4.728	6.180	1.775	0.663	3.384	15.670	
Balance	1.317	0.684	2.592	0.643	0.219	0.444	2.287	3 day balance
Balance/d/k	0.032	0.016	0.063	0.015	0.005	0.011	0.055	
Period 9: 25 Drops Daily of Crystalline Vitamin D in Propylene Glycol Plus 15 Cc. of a 10 per Cent Solution of H_3PO_4								
Excretion:								
Urine	0.095	2.020	2.947	1.188	0.080	2.328	10.578	Weight: 13.8 Kg.
Stool	3.319	2.082	0.238	0.078	0.394	—	0.964	Duration of
Total	3.414	4.102	3.185	1.266	0.474	2.328	11.542	period: 7/7-7/13
Intake	3.951	4.161	6.062	1.537	0.585	2.938	13.568	
Balance	0.537	0.059	2.877	0.271	0.111	0.610	2.026	3 day balance
Balance/d/k	0.013	0.002	0.070	0.006	0.002	0.014	0.049	
Period 10: 25 Drops of Crystalline Vitamin D in Propylene Glycol Plus 15 Cc. of a 10 per Cent Solution of H_3PO_4								
Excretion:								
Urine	0.114	1.821	2.040	0.921	0.102	2.289	11.160	Weight: 13.8 Kg.
Stool	2.880	2.070	0.324	0.015	0.387	—	1.263	Duration of
Total	2.994	3.891	2.364	0.936	0.489	2.289	12.423	period: 7/13-7/18
Intake	4.017	4.188	6.327	1.566	0.600	2.970	13.884	
Balance	1.023	0.297	3.963	0.630	0.111	0.681	1.481	3 day balance
Balance/d/k	0.025	0.007	0.095	0.015	0.003	0.017	0.036	
Period 11: Control								
Excretion:								
Urine	0.260	1.428	6.224	1.055	0.185	1.826	11.490	Weight: 14 Kg.
Stool	2.269	1.653	0.314	0.000	0.326	—	1.474	Duration of
Total	2.529	3.081	6.538	1.055	0.511	1.826	12.964	period: 8/2-8/5
Intake	4.535	3.135	6.902	1.763	0.670	3.378	15.515	
Balance	2.006	0.054	0.364	0.708	0.159	1.552	2.551	
Balance/d/k	0.047	0.001	0.009	0.017	0.004	0.037	0.060	
Period 12: $CaHPO_4.2H_2O$								
Excretion:								
Urine	0.217	1.400	9.100	1.037	0.096	2.788	13.060	Weight: 14 Kg.
Stool	6.387	3.506	0.418	0.015	0.588	—	1.886	Duration of
Total	6.604	4.906	9.528	1.052	0.686	..	14.946	period: 10/19-10/22
Intake	7.528	5.478	7.418	1.819	0.701	3.499	16.156	
Balance	0.924	0.572	—2.110	0.767	0.015	0.711	1.210	
Balance/d/k	0.022	0.014	—0.050	0.018	+0.000	0.017	0.029	
Period 13: Crystalline Vitamin D in Propylene Glycol Plus $CaHPO_4.2H_2O$								
Excretion:								
Urine	0.183	1.403	6.663	1.258	0.164	2.988	12.174	Weight: 14 Kg.
Stool	6.000	3.253	0.230	0.007	0.512	—	1.873	Duration of
Total	6.183	4.656	6.893	1.265	0.676	2.988	14.011	period: 10/27-11/2
Intake	7.481	5.434	6.688	1.782	0.682	3.394	15.775	
Balance	1.298	0.778	—0.205	0.517	0.106	0.406	1.764	3 day balance
Balance/d/k	0.031	0.018	—0.005	0.012	0.002	0.010	0.042	

quotient was 0.82 (the child cried during the test). Thirty-five grams of dextrose was administered again, and one and a half hours later the quotient was 0.75.

The results of the following additional studies made on the patient were found to be within normal limits: (1) galactose tolerance tests for hepatic function; (2)

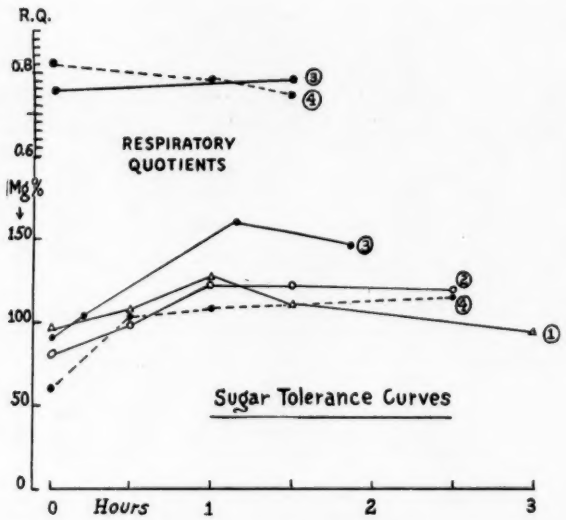

Fig. 3.—Curves representing sugar tolerance and respiratory quotients.

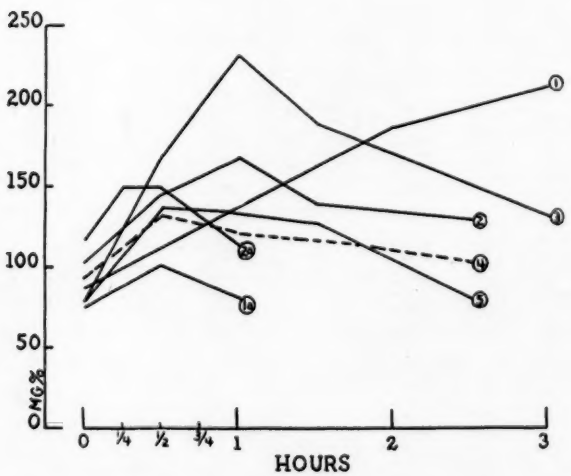

Fig. 4.—Dextrose tolerance and epinephrine curves. Curve *1* represents result of dextrose tolerance test after injection of 5 units of insulin; curve *2*, results after administering 20 units daily for one month; curve *3*, results of no treatment for three months; curve *4*, results after administering lipocaic for ten weeks; curve *5*, results after administering lipocaic for ten months. Curve *1a* represents the epinephrine curve before treatment, and curve *2a* the epinephrine curve after treatment with lipocaic.

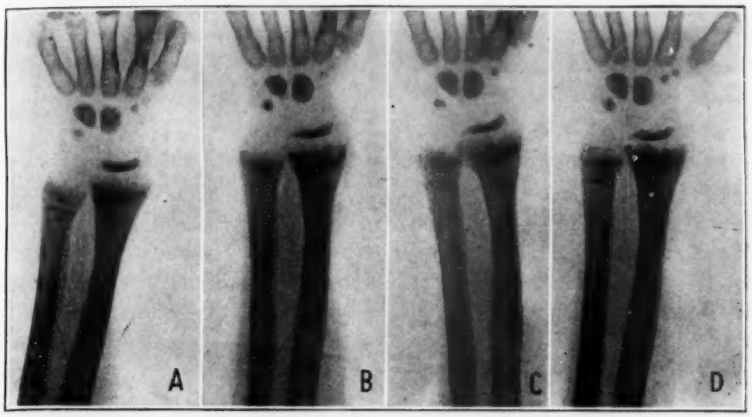

Fig. 5.—Roentgenograms of the wrist taken during different periods of the metabolic study. *A*, taken just before metabolic study was started shows changes similar to those described in figure *1c*, except that an additional center of ossification is visible. *B* and *C* were taken two and three weeks, respectively, after intensive treatment with crystalline vitamin D in propylene glycol. There appear to be no significant changes as compared with those shown in *A*. *D*, taken after three weeks' intensive treatment with vitamin D and two weeks' treatment with both vitamin D and phosphoric acid (640 mg. phosphorus per day), shows some improvement in calcification at the distal ends of the radius and ulna.

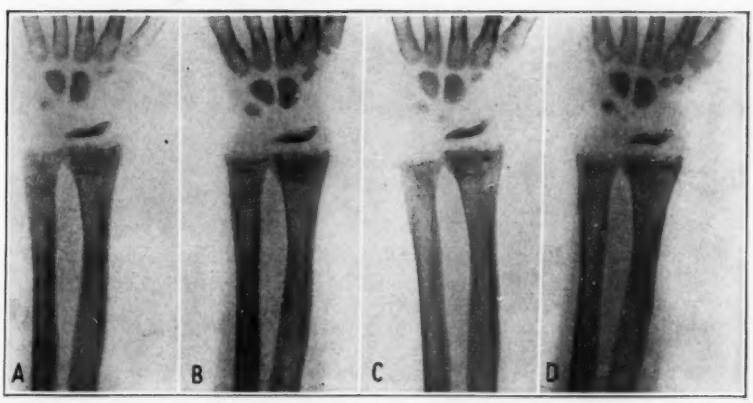

Fig. 6.—Roentgenograms of the wrist taken at different periods of the metabolic study. *A*, taken after one month of therapy with vitamin D and one month with both vitamin D and phosphoric acid, shows little, if any, change in calcification noted in previous roentgenograms. *B* was taken two weeks later, after the child had received phosphoric acid but no vitamin D. *C*, taken after the child had been on a general ward diet for ten weeks without either vitamin D or phosphoric acid, shows no change that would indicate aggravation of the rachitic process. *D* was taken after two weeks' treatment with vitamin D and calcium phosphate. The diet used was the same as in previous metabolic studies. Again, there appears to be no change from previous roentgenograms.

the Hamilton and Schwartz [17] test for the presence of increased amounts of parathyroid hormone in the blood; (3) analysis of stool for neutral fats, fatty acids and soaps; (4) test for gonadotropin in the urine; (5) test for lactic acid in the whole blood, and (6) test for phosphatase in the duodenal secretion.

No estrogenic substance was found in the urine.

Intravenous pyelograms revealed kidneys of normal size and shape. The pelvis and calices of neither kidney showed distortion or dilatation. Neither ureter showed obstruction or kinking.

Since the amount of inorganic phosphorus in the blood did not increase in spite of the administration of vitamin D, phosphoric acid and calcium phosphate, it was hoped that such an increase might be accomplished by thyroid medication.

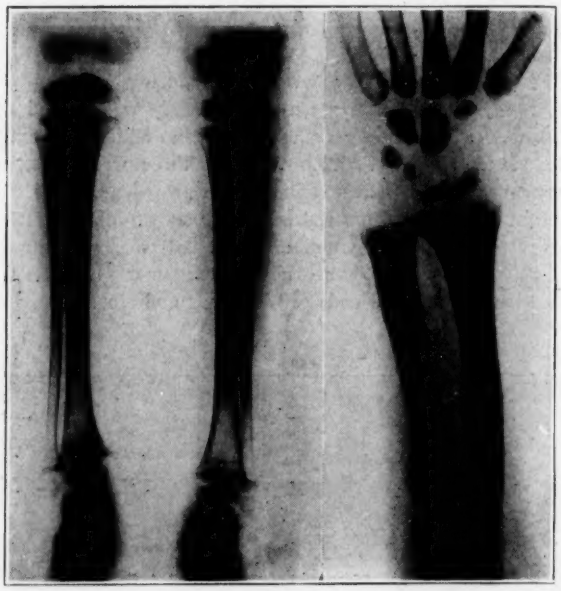

Fig. 7.—Roentgenograms taken eleven months after the initial metabolic period. The child had been at home and had partaken of a general diet plus viosterol in oil, 60 drops daily (13,320 U. S. P. units of vitamin D). These show that, although the bones grew in length and there was some improvement in calcification, the rachitic process still persisted, in spite of several forms of what is considered to be specific therapy.

Accordingly, 1 grain (0.065 Gm.) of thyroid was given daily for a period of two months, but the effect on the level of inorganic phosphorus in the blood and on the healing of the rachitic process in the bones was entirely negative.

17. Hamilton, B., and Schwartz, C.: A Method for Determination of Small Amounts of Parathyroid Hormone, J. Pharmacol. & Exper. Therap. **46**:285, 1932; Rickets and Hyperparathyroidism, Am. J. Dis. Child. **46**:775 (Oct.) 1933.

Because of the acetonuria and the sustained blood sugar curves after the administration of dextrose, 20 units of insulin was administered daily for a period of one month. The diet was not restricted. This therapy resulted in disappearance of acetone bodies from the urine but was without effect on the excretion of sugar or the carbon dioxide–combining power of the blood. The liver still remained enlarged.

The acetonuria, hyperlipemia, acidosis and response to insulin seemed to indicate that the hepatomegaly was due to infiltration of the hepatic cells with fat, such as is sometimes encountered in experimental pancreatic diabetes [18] and in some cases of severe juvenile diabetes treated with seemingly proper diets and adequate amounts of insulin.[19] In these diabetic states, the fatty infiltration of

Fig. 8.—Roentgenograms taken after the administration of sodium phosphate for over two months. The findings in the metaphyses are similar to those in previous roentgenograms, and marked osteoporosis is evident.

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18. (*a*) Fisher, N. F.: Attempts to Maintain Life of Totally Depancreatectomized Dogs Indefinitely by Insulin, Am. J. Physiol. **67**:634, 1924. (*b*) Allen, W. F.; Bowrie, J. J.; Macleod, J. J., and Robinson, W. L.: Behaviour of Depancreatized Dog Kept Alive with Insulin, Brit. J. Exper. Path. **5**:75, 1924. (*c*) Van Prohaska, J.; Dragstedt, L. R., and Harms, H. P.: The Relation of Pancreatic Juice to the Fatty Infiltration and Degeneration of Liver in Depancreatized Dogs, Am. J. Physiol. **117**:166, 1936.

19. (*a*) Hanssen, P.: Enlargement of the Liver in Diabetes Mellitus, J. A. M. A. **106**:914 (March 14) 1936. (*b*) White, P.: Diabetes in Childhood and Adolescence, Philadelphia, Lea & Febiger, 1932, p. 169. (*c*) Grayzel, H. G., and Radwin, L. S.: Hepatomegaly in Juvenile Diabetes Mellitus Treated with Pancreatic Extract, Am. J. Dis. Child. **56**:22 (July) 1938.

the liver can be prevented or cured by adding to the diet either whole pancreas [20] or an alcoholic extract of raw pancreas, which was named lipocaic by Dragstedt and his associates. We therefore tested the effects of this extract on our patient for a period of ten months, without restriction of diet or administration of insulin. This therapy produced only moderate reduction in the size of the liver, but it definitely caused the disappearance of acetone from the urine, the return of the blood sugar curve to a more normal pattern and a reduction of the concentration of the ketone bodies in the blood (fig. 4). The significance of these changes will be discussed presently.

Fig. 9.—Appearance of the patient (left) at the age of 7½ years, and that of her sister, aged 3½ years.

The roentgenograms of the bones, taken at frequent intervals, showed but slight deposition of lime salt in the rachitic metaphyses, and although the long tubular bones increased in length during the period of observation, the shafts remained osteoporotic and the ends showed evidence of active rickets (figs. 5, 6,

20 Dragstedt, L. R.; Van Prohaska, J., and Harms, H. P.: Observations on a Substance in Pancreas (a Fat Metabolizing Hormone) Which Permits Survival and Prevents Liver Changes in Depancreatized Dogs, Am. J. Physiol. **117**:175, 1936. Allen, Bowrie, Macleod and Robinson.[18b] Grayzel and Radwin.[19c]

7 and 8). The roentgenographic appearance of the bones, therefore, was in harmony with the metabolic and clinical observations.

In order to overcome the acidosis, we administered to our patient citric acid-sodium citrate buffer solutions in amounts of 60 cc. daily over a period of three months. The level of phosphorus in the blood was uninfluenced, and roentgenograms of the long bones showed no evidence of increased calcification. The administration of sodium phosphate (Na_2HPO_4) in amounts of about 5 Gm. daily for more than a period of two months did not result in healing of the rachitic process or increase in the level of phosphorus in the blood; but we noted increased osteoporosis.

COMMENT

During childhood chronic glomerular nephritis of long standing has been recognized as an etiologic factor in the production of rachitic-like changes in the long bones (renal rickets), but Fanconi has recently described rachitic lesions in cases in which the only renal changes observed were in the tubules. In naming this condition "der frühinfantile nephrotisch-glycosurische Zwergwuchs mit hypophosphatämischer Rachitis," he associated this form of rickets with nephrosis.

The clinical and metabolic studies just cited clearly indicate that the patient under discussion is not suffering from renal rickets. Also, from available clinical and chemical evidence, we are unable to deduce that this child is suffering from the Munk type of nephrosis. We found no lowering of the concentration of protein in the blood serum and no reversal of the albumin and globulin ratio. There was no marked hypercholesteremia, and anisotropic lipoid bodies could not be demonstrated in the urine. She never showed any edema, nor was there any evidence of increased susceptibility to pneumococcic or streptococcic infection. The only abnormal findings in her urine were slight albuminuria and cylindruria.

These findings denote pathologic changes in the renal epithelium, which may be the result of a necrotizing form of nephrosis or of some metabolic disorder. In the necrotizing type of nephrosis, in which metabolic disorders result from changes taking place in the renal tubules, it may be stated that the severity of the symptoms parallels the degree of renal damage. Our patient has a profound metabolic disturbance, but the amount of pathologic change in the renal tubules, in the absence of manifest signs of disturbance of renal function, must be slight indeed. Besides, the ordinary causes of this type of nephrosis are absent; that is, we have no history or chemical evidence of chronic poisoning with heavy metals or of a long-standing suppurative process.

Of the severe metabolic disorders that may produce degenerative changes in the parenchyma of the kidney, diabetes mellitus may be cited as an example. But this disease usually occurs in arteriosclerotic persons or in those suffering from preexisting renal disease. Even in these patients the nephrotic syndrome that supervenes may be the result of the starvation treatment. It is therefore not clear whether such metabolic

disorders, per se, ever bring about the so-called nephrotic syndrome. There is, however, good evidence that the renal parenchyma shares in the general bodily changes that occur in diabetes mellitus; that is, fatty infiltration and deposits of glycogen in the cells lining the renal tubules are observed. The renal damage resulting is, therefore, a secondary phenomenon.

We may therefore explain the albuminuria in our patient on the supposition that the metabolic disorder slightly altered the permeability of the renal epithelium to albumin and permitted small quantities of albumin to appear in the urine. This alteration in the cells lining the renal tubules was, however, a "by-product" of the metabolic disturbance and did not play any role in the causation of the disease under discussion.

Albright and associates [21] and McCune [22] have reported cases of refractory rickets in which, in order to obtain evidence of healing roentgenologically and serologically, it was necessary to give huge doses of vitamin D (1,500,000 U. S. P. units). Our case differs from theirs in the following respects: 1. The patient responded to administration of vitamin D (6,250 U. S. P. units) like a patient in the healing stage of infantile rickets in that she diverted the excretion of phosphorus from the bowel to the urinary tract and was capable of retaining calcium and phosphorus in a 2:1 ratio. 2. The level of phosphorus in her blood serum could not be raised, even when huge doses of vitamin D were administered (3,000,000 U. S. P. units). We can, therefore, exclude the presence in our patient of resistance to ordinary amounts of vitamin D.

Gerstenberger [23] has described rachitic changes in the long bones of infants suffering from severe hepatic damage. Two of his patients had congenital malformations of the biliary system, and 1 showed advanced cirrhosis of the liver. These children failed to respond favorably to vitamin D therapy. The factor responsible for the rachitic process in his patients was, therefore, either a failure on the part of the body to supply the essential biliary salts necessary for the proper absorption of calcium and phosphorus [24] from the intestinal tract or a diseased liver incapable of storing or utilizing vitamin D. Neither of these factors operated in our patient. She at no time showed any jaundice; the concentration of urea and fibrinogen in the blood were normal; the curves for epinephrine seemed to indicate adequate mobilization and utilization of glycogen. The vitamin D content of the blood of our patient showed

21. Albright, F.; Butler, A. M., and Bloomberg, E.: Rickets Resistant to Vitamin D Therapy, Am. J. Dis. Child. **54**:529 (Sept.) 1937.

22. McCune, D. T.: Resistant Rickets in Twins, read at the annual meeting of the American Pediatric Society, Skytop, Pa., April 27-29, 1939.

23. Gerstenberger, H.: Rachitis hepatica, Monatschr. f. Kinderh. **56**:217, 1933.

24. Greaves, J. D., and Schmidt, L. A.: Further Experiments on the Rôle Played by Bile in the Absorption of Vitamin D in the Rat, Univ. Calif. Publ. Physiol. (no. 5) **8**:43, 1934. Heyman.[14]

a higher level than that of a comparable normal control subject. We can therefore state that in all likelihood the liver did not play any primary role in the causation of this metabolic disturbance.

The activity of the parathyroid glands is closely related to the processes of calcification. Abnormally large amounts of parathyroid hormone in the blood may produce an immediate effect on the concentrations of calcium and phosphorus in the blood serum and eventually lead to demineralization of the skeleton, with the formation of osteitis fibrosa cystica.[25]

Selye [26] and Shelling [27] have shown that the administration of parathyroid extract to young animals fed a moderately rachitogenic diet (calcium-phosphorus ratio 2:1) produces a severe form of rickets which does not respond to vitamin D therapy. The roentgenograms of our patient show no evidence of osteitis fibrosa cystica. We found no increased amount of parathyroid hormone in her blood when this was assayed by the method of Hamilton and Schwartz. The studies on mineral metabolism showed that the excretion of phosphorus and calcium was mostly through the bowel, while in hyperparathyroidism the excretion of these minerals is mainly through the kidneys.

It has been shown that the thyroid gland plays an important role in the metabolism of calcium and phosphorus. Aub and his associates [28] have shown that in myxedema there is a marked calcium retention, while the reverse is true in exophthalmic goiter. Kunde and Carlson [29] and Kunde and Williams [30] produced a rachitic-like disturbance in cretinous animals (rats and rabbits). This form of rickets is resistant to antirachitic therapy. In these instances of perversions of calcification,

25. Jaffé, H. L., and Bodansky, S.: Experimental Fibrous Osteodystrophy (Ostitis Fibrosa) in Hyperparathyroid Dogs, J. Exper. Med. **52**:669, 1930. Johnson, J. L.: Experimental Chronic Hyperparathyroidism, Am. J. M. Sc. **183**:161, 1932. Shelling, D. H.; Asher, D. E., and Jackson, D. A.: Calcium and Phosphorus Studies: Variations of Dose of Parathormone and Calcium and Phosphorus Ratio in the Diet, Bull. Johns Hopkins Hosp. **53**:348, 1933. Greenwald, T., and Gross, J.: The Effect of Long Continuous Administration of Parathyroid Extract upon the Excretion of Calcium and Phosphorus, J. Biol. Chem. **68**:325, 1926. Albright and Ellsworth.[11]

26. Selye, H.: On the Stimulation of New Bone Formation with Parathyroid Extract and Irradiated Ergosterol, Endocrinology **16**:547, 1932.

27. Shelling, D. H.: The Parathyroids in Health and Disease, St. Louis, C. V. Mosby Company, 1935, pp. 104-106.

28. Aub, J. C.; Bauer, W.; Heath, C., and Ropes, M.: Calcium and Phosphorus Studies: The Effects of the Thyroid Hormone and Thyroid Disease, J. Clin. Investigation **7**:97, 1929.

29. Kunde, M., and Carlson, A.: Experimental Cretinism: A Rachitic-Like Disturbance in Extreme Hypothyroidism, Am. J. Physiol. **82**:630, 1927.

30. Kunde, M., and Williams, L.: Experimental Cretinism: The Influence of Thyroid Gland on the Production and Control of Experimental Rickets, Am. J. Physiol. **83**:245, 1927.

whether clinical or experimental, resulting from a disturbance in thyroid function, other symptoms and signs of a disordered thyroid gland are manifest. There is dwarfism. The basal metabolic rates are markedly below normal. Values for cholesterol in the blood plasma are abnormally high. Myxedema or cretinism is usually present. While it is true that our patient is dwarfed, she fails to give any other evidence of thyroid deficiency. We have followed the appearance and development of the centers of ossification in her case. Their number and character are like those found in normal children of similar age. Basal metabolic studies made on our patient gave normal values (+ 10). Numerous determinations of cholesterol in the blood were well within the normal limits for her age. She has never shown signs of myxedema. Her intelligence is that of a normal child of her age. In spite of these negative findings, we gave her 1 grain (0.065 Gm.) a day of whole desiccated thyroid gland over a period of two months and found that this therapy had no beneficial effect on either the concentration of phosphorus in the blood serum or the processes of calcification in the bones. Our findings would therefore absolve this gland from any participation in the formation of the syndrome under discussion.

The fat partition in the stools of our patient showed a normal relation between neutral fats and fatty acids. The enzyme concentrations in the duodenal secretions were within normal limits. We may therefore assume that the external secretion of the pancreas is normal. There was evidence, however, of some dysfunction of the internal pancreatic secretions. The patient had persistent glycosuria, and this partially responded to insulin therapy. She also showed the constant presence of acetone bodies in the urine. The latter completely disappeared on insulin therapy. That underlying these findings is some deep-seated metabolic derangement is further borne out by the low respiratory quotients. These certainly indicate a disturbance in fat, and probably also in carbohydrate, metabolism. The dextrose tolerance curves in the main showed a tendency toward the so-called diabetic plateau. She did not, however, behave like a patient with juvenile diabetes. On a normal diet she did not tend to show aggravation of the disturbance in carbohydrate metabolism; that is, the amount of dextrose excreted in the urine was not increased. Moreover, studies on subjects with juvenile diabetes have never disclosed any rachitic-like changes in their bones or the presence of chronic hypophosphatemia. We are therefore not dealing here with an instance of diabetes mellitus of pancreatic origin. The patient did, however, respond favorably to lipocaic therapy. When this pancreatic extract was administered the level of the total lipids and the acetone bodies in the blood serum fell to normal and the bicarbonate concentration in the serum rose to nearly normal levels. The enlargement of the liver was also favorably influenced by lipocaic therapy. Its size diminished, showing that we were dealing with an abnormal deposi-

tion of fat in the liver, found in many cases of rather severe or poorly managed diabetes mellitus in human beings or in pancreatectomized dogs.

We must therefore assume a disturbance in the internal secretion of the pancreas, in some way analogous to that found in diabetes mellitus but differing from it in many important essentials.

Chown [31] has reported a case of rachitic-like changes in the bones associated with malformation of the anterior portion of the pituitary. This author has also observed other instances in which rachitic-like changes in the long bones were associated with hypophosphatemia, hypercalcemia and reduced renal function but with no direct evidence that the pituitary was involved. He, however, found no evidence of either primary or secondary hyperparathyroidism to explain this syndrome. He therefore suggested the possibility that a pituitary dysfunction may be responsible for the disorder in calcification that occurred in his patients. This author did not, however, mention the presence of either hyperlipemia or acetone bodies in the urine of his patients.

Burn and Ling [32] noted that injections of extracts of the anterior lobe of the pituitary gland resulted in an increased excretion of ketone bodies in rats on a filtered butter diet. Hoffmann and Anselmino [33] found an increased content of ketone bodies in the blood of rats after the injection of extracts of the anterior body of the pituitary gland. Best and Campbell [34] confirmed and extended these observations. The latter authors found not only an increase in the excretion of ketone bodies in the rats given injections of these extracts but also a striking increase in the size and fat content of the liver of these experimental animals.

We were unable to demonstrate roentgenographically an enlargement of the sella turcica. The dextrose tolerance curves did not resemble those associated with dysfunctions of the pituitary gland. The gonadotropic principle was present in normal amounts in our patient's urine. Estrogenic substances were absent from her urine. There was also neither an abnormal absence nor presence of fat in her subcutaneous tissues. These findings tend to rule out an aberration in the function of the pituitary as a cause of the metabolic disorder under discussion. Yet, the dwarfism (definitely not of thyroid origin), the persistence of glycosuria, acetonuria, chronic acidosis (acetonemia) and hyperlipemia (not on a "simple" pancreatic diabetes basis) point to the pituitary as a

31. Chown, B.: Renal Rickets and Dwarfism: A Pituitary Disease, Brit. J. Surg. **23**:552, 1936. Chown, B., and Lee, M.: Renal Rickets and Dwarfism as a Pituitary Disease, Am. J. Dis. Child. **53**:117 (Jan., pt. 1) 1937.

32. Burn, J. H., and Ling, H. W.: Ketonuria in Rats, J. Physiol. **65**:191, 1928; Ketonuria in Rats on a Fat Diet (*a*) After Injection of Pituitary (Anterior Lobe) Extract, (*b*) During Pregnancy, ibid. **69**:xix, 1930.

33. Hoffmann, F., and Anselmino, K. J.: Das Fettstoffwechselhormon des Hypophysenvordeslappens; Stoffwechselwirkungen und -regulationen des Hormons, Klin. Wchnschr. **10**:2383, 1931.

34. Best, C. H., and Campbell, J.: Anterior Pituitary Extract and Liver Fat, J. Physiol. **86**:190, 1936.

possible focus of the metabolic disorder in our patient. It is the ketosis thus produced that enables us to explain tentatively her inability to concentrate phosphate in the body fluids at a level consistent with normal healing. This ketosis, we believe, is the cause of her chronic acidosis. Butler and associates [35] have reported a case of rickets in a 10 year old child. This patient had hypophosphatemia and chronic acidosis. Acidosis in this child was caused by hyperchloremia. Albright, we learned from an unpublished report, had a similar case. The instances cited by these authors and the one which we are reporting have in common rickets, acidosis and hypophosphatemia. It does not matter, apparently, what causes the acidosis. In our case acidosis was not due to hyperphosphatemia or hyperchloremia. The lactic acid content of the blood was normal. There was hyperketonemia, and this, we believe, was responsible for the acidosis.

The persistent rachitic changes in our patient were therefore not due to the primary disturbance in calcification one finds in infantile rickets but seem to have been secondary to a metabolic disorder, probably arising from a dysfunction of the anterior portion of the pituitary gland. This disorder manifested itself in the production of hyperketonemia and hepatomegaly. The ketosis was associated with a persistently low carbon dioxide–combining power of the blood. This acidosis prevented a sufficient concentration of phosphorus in the blood serum to sustain a level consistent with continuous normal calcification.

SUMMARY

A case of rickets associated with dwarfism, glycosuria, ketonuria, lipemia, albuminuria and chronic acidosis is reported.

Studies of the balance of calcium, phosphorus, sodium, potassium, chloride, magnesium and nitrogen were carried out.

Observations on carbohydrate and fat metabolism were made. Biologic and chemical tests to determine dysfunction of the parathyroids, thyroid, pancreas and pituitary were performed.

The pancreas and the pituitary were the only glands of internal secretion in our case which showed some evidence of dysfunction.

This dysfunction manifested itself in a disturbance of carbohydrate and fat metabolism, resulting in chronic ketosis and acidosis, hepatomegaly, glycosuria and dwarfism.

The acidosis was probably responsible for the chronic hypophosphatemia and the rachitic changes in the bones.

The albuminuria and cylindruria can be explained on the basis of changes in the renal epithelium secondary to a primary metabolic disorder.

35. Butler, A. M.; Wilson, J. L., and Farber, S.: Dehydration and Acidosis with Calcification at Renal Tubules, J. Pediat. **8**:489, 1936.

INTESTINAL OBSTRUCTION FROM INSPISSATED MECONIUM

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Several cases of intestinal obstruction in the newborn due to meconium have been reported. Some have termed the condition "meconium ileus," a name which seems particularly appropriate, as undoubtedly ileus is present at some time in every case and the cause is inspissated meconium.

In these cases the bowel is blocked by thick gummy meconium, and rupture may follow the first feeding. Boyd [1] stated that in a number of cases there has been a congenital stenosis of the opening of the pancreatic duct with dilatation of the duct system and fibrosis of the tissue (Kornblith and Otani [2]) and also that Farber reported in a personal communication that he had observed this pancreatic lesion in twins, both of whom died. Bullowa and Brennen,[3] in 1919, were the first to describe this condition in the newborn. The subject was well summarized by Dodd [4] in 1936. Recently Anderson and Hild [5] reported a case identical in most respects with the following case. It is reasonable to suppose that more cases would be discovered if all infants manifesting symptoms of intestinal obstruction soon after birth could be thoroughly investigated.

REPORT OF A CASE

History.—Baby S., a boy, had an uneventful birth at 1 a. m. May 31, 1939, at home. He cried little and slept well until 7 a. m., refusing to nurse at that time. At 9 a. m. he nursed and throughout the day took water well, though he vomited several times. He refused to nurse again until 5 p. m. He voided several times throughout the day but passed no stool. This worried the mother. The following morning, thirty hours after birth, the visiting nurse attempted to induce a bowel movement by use of a soap stick; only two or three small

1. Boyd, W.: Text-Book of Pathology, ed. 3, Philadelphia, Lea & Febiger, 1938, p. 567.

2. Kornblith, B. A., and Otani, S.: Meconium Ileus with Congenital Stenosis of the Main Pancreatic Duct, Am. J. Path. **5**:249 (May) 1929.

3. Bullowa, J. G. M., and Brennen, R. E.: Intra-Uterine Intestinal Obstruction from Inspissated Meconium, J. A. M. A. **73**:1882 (Dec. 20) 1919.

4. Dodd, K.: Intestinal Obstruction Due to Meconium Ileus in a New Born Infant, J. Pediat. **9**:486 (Oct.) 1936.

5. Anderson, E. W., and Hild, J. R.: Meconium Ileus, J. A. M. A. **112**:2275 (June 3) 1939.

hard lumps of fecal material were obtained. The abdomen was distended at this time. A dose of castor oil and an enema gave no results. Thirty-six hours after birth the baby was regurgitating everything he took by mouth. He was admitted to the Camden-Clark Memorial Hospital, and an attempt was made to secure a movement with an oil enema, with no results. The abdomen was tense and tympanitic. It was quiet; no peristalasis was present. A mass the size of a dill pickle and of a somewhat similar shape was palpated in the right side of the abdomen. A flat roentgen plate demonstrated much gas in the bowel. A barium sulfate enema showed the colon to be collapsed and the cecum to be in the upper right quadrant of the abdomen (fig. 1). No barium passed into the ileum. A tentative diagnosis of intestinal obstruction due to volvulus of the terminal portion of the ileum associated with malrotation of the intestine was made.

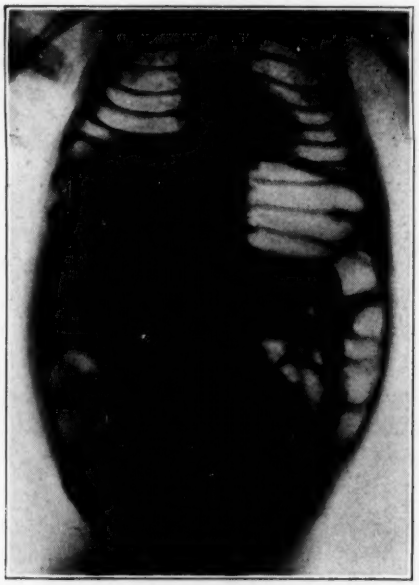

Fig. 1.—Roentgenogram taken after a barium sulfate enema which shows the collapsed colon and the presence of the cecum in the right upper quadrant of the abdomen.

Operation.—At operation under abdominal wall block, induced with a 1 per cent solution of procaine hydrochloride, through a right rectus incision a distended, conical segment of ileum, 2 feet (61 cm.) long and 2 inches (5 cm.) in diameter, was delivered. The segment was rather firm and felt as though its contents were of a thick, tenacious, putty-like consistency. The walls of the segment were thickened and hypertrophied. The ileum above was distended with fluid and gas, and the intestinal wall was thin. The ileum below the segment was completely empty, contracted, firm and about the size of an ordinary pencil.

It was apparent that this large mass could not be removed by enterotomy; so a resection of the segment (fig. 2) with end to end anastomosis was done. The small distal segment was made to fit the large upper segment by splitting it for a distance of 1 cm. down to its antimesenteric border. The baby stood the

operation well. Immediately after operation 50 cc. of citrated blood was transfused. The following day the abdomen was moderately distended. The stomach was kept empty by gastric lavage every two hours. Five hundred cubic centimeters of 5 per cent dextrose in a physiologic solution of sodium chloride was given by hypodermoclysis daily. A second transfusion of 25 cc. of blood was given on the second postoperative day. Fluids by mouth were started on the third postoperative day, and regurgitation occurred frequently. The baby became progressively weaker and died on the fourth postoperative day, without having had a bowel movement.

Fig. 2.—Segment of ileum, 2 feet (61 cm.) long and from 1½ to 2 inches (4 to 5 cm.) in diameter, removed at operation on a child 1½ days old.

Pathologic Report (Dr. A. R. K. Matthews).—The liver was markedly congested. The common bile duct was patent. The pancreas was small, measuring about 2.5 cm. in length and 1 cm. in diameter, shaped like a crescent and lying in the curve of the duodenum. It weighed 1.5 Gm. (normal weight at birth, 4 to 4.5 Gm.). On section it showed nothing unusual. The ampulla of Vater was prominent. The ducts of Wirsung and Santorini could not be identified grossly.

Microscopic Examination.—Pancreas: The pancreas showed a large amount of loose fibrous connective tissue between the lobules of glandular tissue. The acini of the gland were frequently filled with large eosin-staining epithelial cells; others contained formless eosin-staining material, and the smaller ducts were filled with similar material. Many of these ducts were so markedly dilated and distended that

the presence of some obstruction would seem probable. There was some chronic inflammatory reaction in the surrounding connective tissue, and a small hyperplastic lymph node was present. These findings added further evidence in favor of the theory of a congenital defect in the pancreatic duct which had been suggested by the gross examination.

Liver: The hepatic cells were pale and granular; some bile pigment was present, and some of the biliferous canaliculi contained small plugs of dark yellowish material.

COMMENT

As yet no patient with obstruction from inspissated meconium is reported as having recovered by either medical or surgical treatment. The cause of the condition has been shown in some cases to be due to congenital stenosis of the pancreatic duct, leading to absence of the pancreatic juice and failure to digest the fats and proteins of the meconium. The meconium in turn becomes thick, gummy and putty-like and leads to intestinal obstruction.

SUMMARY

A case is reported in which the meconium, thick, gummy and wax-like, had caused an intestinal obstruction. The obstruction was relieved by operation, but recovery was precluded by the congenital anomalous absence or fibrosis of the terminal portion of the pancreatic duct system, with obstruction and atrophy of the pancreatic tissue and resultant failure of pancreatic secretion.

WINCKEL'S DISEASE

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Winckel's disease is a malady of the newborn of unknown origin, characterized by the symptom complex of jaundice, cyanosis and hemoglobinuria. Because of this triad and the fact that the course of the disease is usually afebrile, Winckel [1] suggested that the condition be called "cyanosis afebrilis icterica perniciosa cum haemoglobinuria." While this name adequately describes the main symptoms of the disease, as well as gives the prognosis which has been usual at least until recently, it is too cumbersome for general use, and there is no reason why the eponym "Winckel's disease" should not be employed. The only real objection is the fact that the condition was indubitably seen and described by others previous to Winckel, though not with his emphasis on the major symptoms.

The etiologic factor in Winckel's disease is usually assumed to be toxemia, either bacterial or chemical, more probably bacterial. Syphilis has not been considered an etiologic factor. The essential pathologic changes consist of icterus and multiple punctate hemorrhages in all organs, including the brain and spinal cord. The blood changes to a chocolate brown, the white cells are moderately increased and the hemoglobin content is markedly reduced. The urine is greenish brown and contains numerous red blood cells and large amounts of hemoglobin and methemoglobin. Bile pigment is usually absent. The disease generally starts between the ages of 4 and 12 days, with sudden onset of icterus, which becomes progressively more intense. Polyuria develops, and the urine is stained with blood pigment. Fever is not particularly common, but restlessness, cyanosis and rapid pulse and respirations occur. Death may occur in a few hours but not usually before a few days, occasionally as late as two weeks after onset of the disease. The mortality is extremely high. The chief conditions from which Winckel's disease must be differentiated are erythroblastosis foetalis, icterus gravis neo-

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1. von Winckel, F.: Ueber eine bisher nicht beschriebene endemisch aufgetretene Erkrankung Neugeborener, Deutsche med. Wchnschr. **5**:303, 1879.

natorum, Buhl's disease, congenital heart disease and Lederer's anemia. The diagnosis, however, is usually not difficult because of the characteristic triad: icterus, cyanosis and hemoglobinuria. The clinical and pathologic features of Winckel's disease have been thoroughly reviewed by Polayes and Kramer,[2] to whom reference should be made for further details.

The reason that Winckel's disease has all but disappeared in recent years is doubtless the decline of sepsis of the newborn during this period. This opinion was expressed by Grulee and Bonar,[3] who stated that nearly all cases were seen before strict asepsis was observed in the conduct of labor. In confirmation of their observation and as an indication of the inadequacies of the care of the newborn during that period, it is interesting that it was noted in the protocols that 12 of the 14 patients with a disease described by Charrin[4] under the name of "maladie bronzée hématique des enfants nouveau-nés" had thrush. Charrin's contribution will be further discussed.

Winckel's disease apparently began to emerge as a nosologic entity when Pollack,[5] in 1871, described a number of infants with hematuria and jaundice. Of 12 patients observed during one year, only 2 recovered. It is not, however, beyond possibility that none of these had what one would now classify as Winckel's disease, because he did not mention the symptom of cyanosis and stated that most of the patients were over 6 weeks of age, which is much later than the age at which Winckel's disease usually begins. Pollack expressed the belief that the principal symptom, hematuria, was secondary to thrombosis of the renal veins following gastroenteritis. Parrot,[6] in 1873, described 2 cases of what was probably Winckel's disease, which he called "tubulhématie rénale chez des nouveau-nés." Parrot mentioned Pollack's communication and apparently believed he was describing the same disease. He mentioned having seen an autopsy by Vulpian in a similar case in 1861. Parrot expressed the belief that the causation was a primary blood dyscrasia.

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2. Polayes, S. H., and Kramer, B.: Winckel's Disease: Report of Case; Repeated Transfusion; Recovery, J. Pediat. **2**:482, 1933.

3. Grulee, C. G., and Bonar, B. E.: Winckel's Disease, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1939, vol. 1, chap. 42, p. 107.

4. Charrin, S.: Maladie bronzée hématique des enfants nouveau-nés (tubulhématie rénale de M. Parrot), Thesis, Paris, no. 442, 1873.

5. Pollack, O.: Ueber Nierenblutung im Säuglingsalter, eine Nachkrankheit des Darmkatarrhes, Wien. med. Presse **12**:458, 1871.

6. Parrot, J.: Sur deux cas de tubulhématie rénale chez des nouveau-nés, Arch. de physiol. **5**:512, 1873.

Laroyenne,[7] who has been credited with first describing this condition,[8] reported a case in 1873 but stated that a similar case had been previously described by Parrot. Charrin [4] over a period of one year observed 14 cases, in all of which the termination was fatal. Some of these might not now be accepted as cases of Winckel's disease, because in 6 instances hematuria was not mentioned in the protocols during life nor was grossly bloody urine found in the bladder on necropsy. However, blood was found microscopically in the renal tubules in every instance. In 1 case, also, cyanosis was not mentioned. However, there is no doubt but that most of these were cases of Winckel's disease. The rapidity with which death may occur is illustrated by case 9 of Charrin's series. He was called back to the ward one-half hour after having completed rounds to see an infant girl, 6 days of age, who had appeared normal during rounds but in the brief interval which had elapsed had suddenly become acutely icteric and critically ill. The child died four hours after the onset of jaundice. Charrin concluded that he was describing the same disease as that reported by Pollack and Parrot but stated that the causation was not yet established.

Winckel,[1] in 1879, reported the first of the infrequent epidemics of the disease. This involved 23 infants, of whom 19, or 82 per cent, died. The shortest duration in any case was nine hours. A number of cases have since been reported, and in 1933 the literature was reviewed by Polayes and Kramer,[2] who added a case of their own. Their patient recovered after blood transfusion, the first reported use of this therapeutic procedure in the disease. A case of fatal termination was reported by Wheeling and Slesinger [9] in 1934. There is some doubt, however, as to whether the latter should be considered a true case of Winckel's disease, as there was no examination of the urine reported and large hemorrhagic areas were observed throughout the adrenal glands at necropsy. Dop,[10] who reported on a patient in 1939 who recovered after the repeated intramuscular injection of whole blood, stated that adrenal hemorrhage could not be ruled out as the cause of death in the case of Wheeling and Slesinger. However, there may be various immediate causes of death in this form of sepsis, and there is no reason, in view of the tendency to bleeding, why adrenal hemorrhage should not be one of them.

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7. Laroyenne: Sur une maladie nouvelle des nouveau-nés, Assoc. franç. p. l'avance. d. sc., Compt. rend. **2**:877, 1873.

8. Feldman, W. S.: A Case of So-Called Winckel's Disease, Brit. J. Child. Dis. **24**:113, 1927.

9. Wheeling, W. S., and Slesinger, H. A.: Winckel's Disease: Report of Case, Arch. Pediat. **51**:740, 1934.

10. Dop, P. H.: A Case of Winckel's Disease with Recovery, Acta pædiat. **23**:397, 1939.

Our case of Winckel's disease is the first ever observed in Strong Memorial Hospital. We feel that it is worthy of reporting because our patient, like the patients of Polayes and Kramer and Dop, recovered after the parenteral administration of blood. For this reason we cannot feel that the prognosis is as hopeless as that expressed by Grulee and Bonar:[3] "There is no treatment of avail except that directed toward hemorrhagic disease. This probably in the nature of things would not be successful." Another reason for reporting our case is that we are able, through the Eastman Kodak Company, to present a photograph of our patient in color which illustrates the cardinal features of this rare condition and is probably the first ever taken in a case of this disease. Other observations, such as the estimation of the degree of jaundice by means of the icteric index, may also be of interest.

REPORT OF A CASE

The infant was a white boy, spontaneously delivered after a normal pregnancy. He weighed 3,140 Gm. (7 pounds) at birth and appeared normal in every way. During the first few days a mild jaundice developed, which was considered physiologic and which had cleared completely by the time he was 12 days of age. He was discharged with an artificial milk formula and was thriving well. The family history was not significant.

Late in the morning of the fourteenth day it was noticed that the child had become icteric. The jaundice deepened rapidly in the next few hours, and he became listless and drowsy. The child was then seen by us and immediately hospitalized. At that time his weight was 3,060 Gm., and the rectal temperature was 37 C. (98.6 F.). He was drowsy, breathed normally and made no cry when disturbed. The sclerotics were icteric, and there was marked generalized icterus, including icterus of the mucous membranes. The icterus seemed less marked on the hands and feet. The spleen was not felt. The liver was normally dull to percussion above the costal margin and down to 2 or 3 cm. below the costal margin. The muscle tone and reflexes were normal.

An intravenous transfusion of 60 cc. of citrated whole blood was given as soon as possible after admission to the hospital. That evening he became cyanotic and was placed in an oxygen box. At that time the probable diagnosis of Winckel's disease was suggested by the symptom complex of jaundice, hematuria, which appeared after admission to the hospital, cyanosis and lack of elevation of temperature. The child appeared so ill that no hopes were entertained for his survival and permission for a necropsy was obtained. Later in the evening he was given 100 cc. of a 5 per cent solution of dextrose subcutaneously. It was noted that the urine, which had become dark and contained considerable blood, was alkaline in reaction. We did not, therefore, feel it necessary to administer alkali to prevent the precipitation of acid hematin in the kidneys. The following morning the child was somewhat improved. He was less jaundiced, and the urine was clearer and less darkly colored. There was a slight serous discharge from the umbilicus, a culture of which later showed diphtheroids. He was given another intravenous transfusion of 60 cc. of citrated whole blood and later in the day 100 cc. of physiologic solution of sodium chloride subcutaneously. Oxygen was again administered that evening because of cyanosis.

A patient with Winckel's disease three days after onset. Details of the photograph are described in the text.

The next morning, the third day of admission, the child seemed to have made considerable improvement. His urine was now free from gross blood; he cried vigorously for the first time since admission and took his feedings well. On this date the accompanying photograph was taken, which illustrates the three cardinal

TABLE 1.—*Results of Examinations of the Urine*

Day of Disease	Color	Reaction	Albumin	Sugar	Acetone	Guaiac	Bile	Microscopic Examination
1	Dark amber	Alkaline	+++	0	+	++++	++++	Many granular casts; 1 to 4 red and white blood cells per high power field
2	Reddish brown	Alkaline	++	0	0	+++	++++	Occasional white and red blood cells; granular debris; casts
3	Dark yellow	Alkaline	+	0	0	++	+	Occasional white and red blood cells
5	Yellow	Alkaline	0	0	0	0	0	Negative
2	No fluorescence under ultraviolet light, indicating absence of porphyrins. Spectroscope showed band for oxyhemoglobin							

TABLE 2.—*Results of Examinations of the Blood*

Day of Disease	Hemoglobin, Gm.	Red Blood Cells	White Blood Cells	Polymorphonuclears	Lymphocytes	Smear	Icteric Index	Other Reactions
1	10.5	3.09	27,400	73	27	No nucleated red cells	167	
2	10.5	2.8	35,000	..	..	.....	240	Direct van den Bergh negative; indirect van den Bergh positive
3	10.0	3.73	.....	..	..	.....	...	
4	12.5	4.54	.....	..	..	.....	120	
5	14.0	4.66	.....	..	..	.....	...	
6	13.5	5.25	22,000	52	48	Appeared normal	...	
7	14.6	4.77	.....	..	..	.....	...	
8	Landsteiner-Donat test for hemolysis on chilling: negative Fragility: 2 and 12 hours; expressed in terms of percentage of solution of sodium chloride; patient 0.32 to 0.44, control 0.34 to 0.44							
9	13.5	4.75	12,000	..	..	.....	...	
10	....	....	.....	..	..	.....	22	Wassermann and Kahn reactions of the blood negative

Other Data

Throat culture on admission: Staphylococcus haemolyticus predominant
Stool on first day of disease dark orange; unchanged bilirubin present (not a normal finding)
Culture of stool on second day of disease: negative for typhoid, paratyphoid and dysentery bacilli
Culture of serous discharge from umbilicus on fourth day of disease: diphtheroids

features of the disease. To the baby's left are three test tubes containing urine: the first, the specimen passed the night of admission; the second, that passed on the second day of admission, and the third, that passed on the third day, when the photograph was taken. The diaper at the baby's right shows the results of a guaiac test on the last specimen of urine. Although the child's condition was greatly improved over that on the first day of admission, the icteric color of the skin and cyanosis may be easily distinguished in the photograph. The boy

was given a third transfusion of 75 cc. of citrated whole blood, and this was repeated on his fourth day in the hospital. By the fifth day the cutaneous jaundice had entirely disappeared, and his urine was free from occult blood. He continued to thrive, but there was still a faint icteric tinge to his sclerotics when he was discharged the tenth day after admission; he weighed at that time 3,360 Gm. Since then the child has thrived brilliantly; he underwent circumcision uneventfully at the age of 9 months and at the age of 1 year was 75 cm. tall and weighed 11.4 Kg.

SUMMARY AND CONCLUSIONS

The literature on the subject of Winckel's disease is briefly reviewed. It is assumed that this is a form of sepsis of the newborn, and until more is known considering its causation there is no good reason why the term "Winckel's disease" should not be used to designate the condition. It is probably important to diagnose the malady early, because in the last 2 unquestioned cases reported in the literature, those of Polayes and Kramer [2] and of Dop,[10] as well as in our case, there was brilliant response to the parenteral administration of blood. Recovery in these 3 cases, from a condition which has had such a uniformly high mortality, suggests that such treatment is the method of choice and should be started as early as possible. A colored photograph of a patient with Winckel's disease is shown, which we believe is the first ever published of this condition.

AGENESIS OF THE CORPUS CALLOSUM

DIAGNOSIS OF A CASE BY ENCEPHALOGRAPHY

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Many obscure disturbances of the central nervous system in infancy and childhood are ascribed to birth injury when disease appears to have been present at birth or in the first months of life or to encephalitis when it appears later. Irish,[1] in a study of 1,000 cases of vascular encephalopathy in which necropsy had been performed, found that 4.4 per cent of the patients were under 20 years of age. Twenty-five of the 40 patients were children under 10 years. A variety of agents were considered to be causative of the condition; in a few instances there was no apparent explanation for the apoplectic death. Obscure cases of hemiplegia in childhood are usually ascribed to encephalitis. Irish pointed out that evidence from anatomic studies fails to substantiate this view, and he concluded that diseased and otherwise defective blood vessels are responsible for most of the focalized neurologic disturbances in childhood.

Without question, primary and secondary vascular disturbances are overlooked in arriving at an etiologic diagnosis of neurologic disturbances. The present report emphasizes the necessity for considering congenital defects of brain structure in determining the cause of obscure cases of epilepsy, feeblemindedness and other neurologic conditions. It also serves to report another case of agenesis of the corpus callosum.

Usually the diagnosis of structural defects of the brain has been speculative. With the advent of encephalography, demonstrations of defective development are being made during life. Such is the case in regard to agenesis of the corpus callosum, which previous to 1934 was recognized only at postmortem examination. In June 1934, at the annual meeting of the American Neurological Association, Hyndman and Penfield [2] read a paper by title reporting 2 cases confirmed by operation; they

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1. Irish, C. W.: Cerebral Vascular Disturbances in Newborn Infants and Young Children, J. Pediat. **15**:64 (July) 1939.

2. Hyndman, O. R., and Penfield, W.: Agenesis of the Corpus Callosum: Its Recognition by Ventriculography, Arch. Neurol. & Psychiat. **37**:1251 (June) 1937.

subsequently brought the total to 5 cases in their publication of 1937. At the same meeting Davidoff and Dyke [3] reported 3 cases in which the diagnosis of agenesis of the corpus callosum was also made during life, with confirmation in 1 instance by pathologic study. It had been reported in two previous publications [4] that the anomalous condition had been discovered in encephalographic films, but the anatomic defect had not been recognized by either author. Since 1937, Köttgen [5] Foerster [6] and Cass and Reeves [7] have reported 3 cases (1 each). The present report brings the number of cases recognized during life to 12.

The embryology and causes of agenesis and the function of the corpus callosum have received thorough consideration most recently by Cass and Reeves.[7] The present discussion will be limited to the details of the roentgenographic diagnosis and clinical symptomatology.

REPORT OF CASE

History.—The subject of this report was 19 months old when he was first seen by one of us (L. R. G.) in December 1938. Information obtained disclosed that the infant, weighing 8½ pounds (3,855 Gm.), had been born spontaneously after a five hour labor May 4, 1937. A swelling on the left side of the head present at birth had grown to tremendous proportions by the ninth day. Subsequently, the swelling ruptured, discharging blood. Secondary infection occurred. The baby was jaundiced and anemic and required several transfusions, but recovered and was discharged from the hospital June 12. The infant had failed to develop normally, required daily enemas and had had four episodes of clonic contractions of the left side of the face and the left arm and leg, initiated by vomiting and followed by exhaustion, irritability and sleepiness. On Oct. 14, 1938, he weighed 22 pounds (10 Kg.), was 31⅛ inches (80 cm.) tall and had sixteen teeth; the anterior fontanel was open. When examined Dec. 15, 1938, he could not feed himself, could not sit alone and did not talk. The occiput was flat and the eyes widely spaced (the same characteristics may be seen in the photograph of the subject of Cass and Reeves's [7] report). Muscular tone and the tendon reflexes were increased on the left, and the Babinski sign was elicited on the left.

When seen at the Wisconsin General Hospital May 29, 1939, he had twenty teeth; the fontanels were closed; he sat alone poorly; his head, which measured 46 cm. in circumference, was rolled aimlessly and he looked unintelligent. The

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3. Davidoff, L. M., and Dyke, C. G.: Agenesis of the Corpus Callosum: Its Diagnosis by Encephalography, Am. J. Roentgenol. **32**:1 (July) 1934.

4. Guttmann, L.: Ueber einem Fall von Entwicklungsstörung des Gross-und Kleinhirns mit Balkenmangel, Psychiat.-neurol. Wchnschr. **31**:453 (Sept. 14) 1929. Dandy, W. E.: Ventriculography Following the Injection of Air into the Cerebral Ventricles, Ann. Surg. **68**:5 (July) 1918.

5. Köttgen, H. U.: Die Erkennung des angeborenen Balkenmangels, Monatschr. f. Kinderh. **78**:227 (May) 1939.

6. Foerster, O.: Ein Fall von Agenesie des Corpus callosum verbunden mit einem Diverticulum paraphysarium des Ventriculus tertius, Ztschr. f. d. ges. Neurol. u. Psychiat. **164**:380, 1939.

7. Cass, A. B., and Reeves, D. L.: Partial Agenesis of the Corpus Callosum: Diagnosis by Ventriculographic Examination, Arch. Surg. **39**:667 (Oct.) 1939.

Fig. 1.—The lateral ventricles show dilatation of the posterior parts of the bodies. The third ventricle is not visualized in this view.

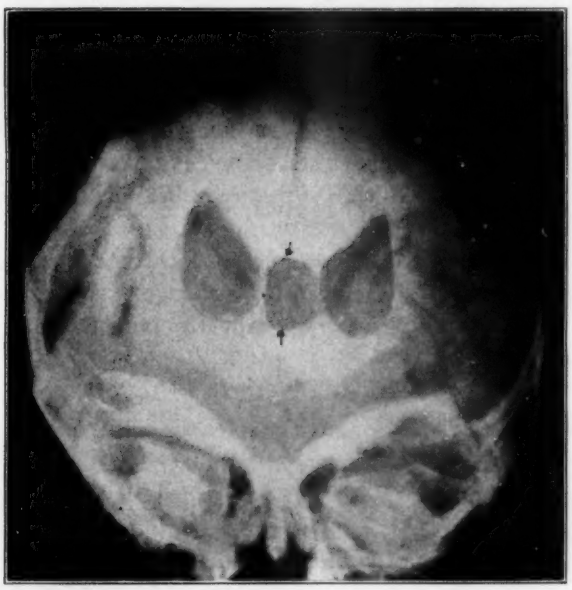

Fig. 2.—Ventricular enlargement, wide separation of the lateral ventricles and dorsal displacement of the third ventricle.

contractions on the left side noted on December 15 were less evident (equivocal). The Wassermann reactions of the blood of the mother and the child were negative.

Encephalography.—The encephalogram showed the posterior portion of the bodies of the lateral ventricles and the posterior horns to be much enlarged, while the anterior horns were much narrower than usual. The temporal limbs were somewhat dilated. There was an unusually wide separation of the lateral ventricles (4.5 cm. measured between the mesial surfaces at the dorsal limit). Between the lateral ventricles and extending much higher than usual was a dilated third ventricle (1.3 by 2.3 cm.). There was no air in the sulci over the convexity of the brain, but air shadows arranged in a radial and dorsoventral direction about the anterior horn were assumed to be on the mesial surface of the hemispheres. The cingulate and callosal sulci were not outlined. The basal cisterns were well filled. The third ventricle could not be visualized in the lateral views.

COMMENT ON THE ENCEPHALOGRAPHIC FINDINGS

The cardinal points in the development of the diagnosis of agenesis of the corpus callosum have been derived by Davidoff and Dyke [3] by comparing the encephalogram of their first patient with the brain at the postmortem examination. As a result, they have enumerated the following dictums as a guide in the encephalographic diagnosis: (1) marked separation of the lateral ventricles; (2) angular dorsal margins of the lateral ventricles; (3) concave mesial borders of the lateral ventricles; (4) dilatation of the caudal portions of the lateral ventricles; (5) elongation of interventricular foramens; (6) dorsal extension and dilatation of the third ventricle; (7) radial arrangement of the mesial cerebral sulci around the roof of the third ventricle and their extension through the zone usually occupied by the corpus callosum. Since the films in the case here described do not conform in all respects to these dictums, chiefly in the absence of the elongated interventricular foramen, this is believed to be an example of partial rather than complete agenesis of the callosal commissure. These dictums of Davidoff and Dyke make it almost impossible to confuse agenesis of the corpus callosum with absence of the septum pellucidum or of the cavum septi pellucidi, which have been described roentgenographically by these two authors.[8]

SYMPTOMATOLOGY

The condition has been found at autopsy in persons of all ages, from the newborn infant to the old person, although most of the cases have been found in children under 10. Retarded development, impaired mentality and epilepsy are the most common clinical manifestations. It is of some interest that 3 of Hyndman and Penfield's 5 patients and all 3

8. Dyke, C. G., and Davidoff, L. M.: Congenital Absence of the Septum Pellucidum: Its Diagnosis by Encephalography, Am. J. Roentgenol. **34**:573 (Nov.) 1935.

of Davidoff and Dyke's patients showed focal epileptic disturbance, as did our patient. This suggests the possibility of an associated defect of the contralateral cerebral hemisphere. The autopsy material has shown that other anomalies of development are frequently associated with agenesis of the corpus callosum. Microcephaly, porencephaly, polygyria, incomplete separation of the frontal lobes and lipoma are among the common associated anomalies. In Foerster's [6] patient the encephalogram revealed, in addition to agenesis of the corpus callosum, a large cyst extending above the third ventricle between the hemihpheres. Operation on this cyst relieved the patient of epilepsy. Reeves and Courville [9] have described a similar condition observed at autopsy. It is altogether possible that the absence of the corpus callosum plays no role in the formation of symptoms and it is rather the associated defects that are responsible for the clinical findings.

SUMMARY

The case of a 19 month old child, defective from birth, clinically manifesting a marked degree of mental enfeeblement and jacksonian epilepsy has been described. The encephalogram revealed during life another instance of agenesis (partial) of the corpus callosum.

9. Reeves, D. L., and Courville, C. B.: Complete Agenesis of the Corpus Callosum: Report of Four Cases, Bull. Los Angeles Neurol. Soc. **3**:169 (Dec.) 1938.

Progress in Pediatrics

MENINGITIS CAUSED BY BACTERIUM COLI ANAEROGENES (ANAEROGENIC COLIFORM ORGANISM)

REPORT OF ITS OCCURRENCE IN A THREE WEEK OLD INFANT, WITH TEMPORARY CORTICAL INSULT AND RECOVERY

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Since the advent of the sulfonamide group of compounds for use in the therapy of infections, reports of recovery from the nonmeningococcic purulent meningitides, a group of diseases hitherto regarded as almost universally fatal, are coming to be looked on as neither startling nor novel. We are presenting in this paper a report of a case of meningitis caused by an anaerogenic coliform organism in a 3 week old infant in which recovery occurred. In addition, we are reviewing some of the literature on this disease. We feel justified in giving a detailed account of the course of our patient's illness, not only because of its gratifying outcome but because a few of its illustrative features are of more than passing interest. Among the subjects which will be discussed are the probable pathogenesis, the bacteriologic observations, the prognosis and the therapy. Finally, because opportunity was afforded to confirm by both electroencephalogram and pneumoencephalogram the presence of cortical changes, reasons for exercising caution in interpretation and for regarding such abnormalities as transient will be stressed.

REPORT OF CASE

History.—R. C., a white girl, was born at full term in a hospital at Monticello, N. Y., on Aug. 5, 1939. The delivery was normal and spontaneous; the weight at birth was 6 pounds 8 ounces (2,955 Gm.). She remanied in the hospital for nine days, and except for the presence of a rash during the first four days and for jaundice, which appeared on the third day, the course was uneventful. From the hospital she was taken to her grandparents' farm in Woodridge, N. Y., where she seemed to thrive on a mixture of water and milk taken directly from the farm's tuberculin-negative cows, to which a preparation of maltose and dextrin was added. On August 25, at the age of 20 days, the infant vomited and began to refuse her

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feedings. She was seen by a local physician and treated with enemas of dextrose and water. After these enemas the infant became pale, rolled her eyes and had several mucoid watery stools. She was brought to Brooklyn twenty hours after the onset of her illness, when she was seen by us. During the trip she vomited repeatedly and hiccuped continuously.

First Admission.—Physical Examination: The patient appeared acutely ill. The temperature was 101 F., the pulse rate was 180, and the respiratory rate 72 per minute. Her voice was shrill and high pitched but became stronger on continued crying. The respirations were grunting, but no cough was present. The skin was pale and of fair turgor, and there was no eruption. The skull was symmetric, and the anterior fontanel, under slight tension, measured 6 by 4 cm.; the posterior fontanel was open and measured 0.5 by 0.5 cm. The pupils were pinpoint in size. There was no eye rolling or strabismus. The nose and ears were normal. There were a few petechiae on the soft palate, and the fauces were injected. No cardiac murmur was audible, and examination of the lungs, except for high-pitched breath sounds at the angle of the left scapula, revealed nothing remarkable. The abdomen was soft, and the liver and the lower pole of the left kidney were just palpable. The spleen was not enlarged. The extremities were normal, and there was no lymphadenopathy. Neurologically, except for the shrill cry and the presence of a slightly positive Kernig sign on the left, the findings were not striking. The diagnoses of possible pneumonia, meningitis, pyelonephritis and septicemia were entertained, and the infant was immediately hospitalized.

Lumbar puncture was performed on admission and cloudy yellowish cerebrospinal fluid removed. In table 1 are summarized the pertinent data from examinations of the spinal fluid throughout the two stays in the hospital (August 26 to October 4 and October 8 to November 8).

Laboratory Data: Examination of the blood on admission showed: hemoglobin content, 88 per cent; red blood cells, 4,300,000 per cubic millimeter, and white blood cells, 14,400, with 78 per cent polymorphonuclears. Urinalysis gave normal results except for a rare white blood cell on microscopic examination. The sedimentation rate was 28 mm. in one hour. The Kline reaction of the blood was negative. A blood culture on admission gave a growth in all mediums, the plates yielding 66 and 98 colonies of an organism identical in all growth characteristics with that isolated from the cerebrospinal fluid, which is discussed later. The count on many repetitions of the examination of the blood during the stay in the hospital revealed that the hemoglobin content ranged from a high of 100 per cent to a low of 56 per cent; the red cell count varied between 5,500,000 and 2,200,000 per cubic millimeter; the white cell count was maintained at a fairly constant level between 17,000 and 13,000 cells, dropping to 5,500 before discharge; the differential count showed a fluctuation in the percentage of polymorphonuclear leukocytes between 78 and 33 per cent.

Bacteriologic Data: The organism recovered from the blood and the cerebrospinal fluid was a hemolytic gram-negative, nonmotile bacillus giving the following reactions in various mediums:

Sugar	Reaction	Gas Formation
Dextrose	Acid	0
Maltose	Acid	0
Mannitol	Acid	0
Lactose	Acid	0
Saccharose	0	0

TABLE 1.—*Data from Examinations of the Cerebrospinal Fluid*

Date	Quantity, Cc.	Appearance	Pressure	Total Cells per Cu. Mm.	Polymorphonuclears, Percentage	Pandy Reaction; Protein, Mg./100 Cc.	Sugar, Mg./100 Cc.	Chlorides, Mg./100 Cc.	Level of Sulfapyridine, Mg./100 Cc.		Smear	Culture
									In Blood	In Cerebrospinal Fluid		
First Admission												
8/26	15	Yellow, purulent	Normal	10,000	95	227	55	407	—	—	Gram-negative diplobacilli	Coliform bacteria
8/27	15	Yellow, purulent	Normal	8,000	92	+++	55	Not determined	—	—	—	Coliform bacteria
8/28	10	Yellow, purulent	Decreased	3,700	86	+++	+	Not determined	8.9	6.4	—	Coliform bacteria
8/29	10	Clear	Decreased	640	60	+++	—	Not determined	8.0	6.1	—	Coliform bacteria
8/31	8	Clear	Decreased	230	51	+++	—	Not determined	7.3	3.9	—	Sterile
9/ 3	12	Xanthochromic	Decreased	310	76	155	27	428	—	3.4	—	Sterile
9/12	6	Bloody	Increased	12,000 (corrected)	85	+++	—	Not determined	—	—	Gram-negative diplobacilli	Coliform bacteria
9/14	15	Bloody	Decreased	1,300	65	+++	—	Not determined	—	—	Gram-negative diplobacilli	Coliform bacteria
9/16	10	Clear	Decreased	280	40	262	23	Not determined	8.1	5.2	—	Sterile
9/18	10	Clear	Decreased	120	0	485	24	423	—	—	—	Sterile
9/20	10	Clear	Decreased	105	0	++++	±	Not determined	—	—	—	Sterile
9/22	7	Clear	Decreased	95	0	++++	35	Not determined	—	—	—	Sterile
9/25	20	Clear	Decreased	90	0	332	35	Not determined	—	—	—	Sterile
9/28	25	Clear	Decreased	46	0	297	29	Not determined	—	—	—	Sterile
10/ 2	10	Clear	Decreased	24	0	+++	45	Not determined	—	2.1	—	Sterile
Second Admission												
10/ 8	15	Clear	Normal	137	60	+++	+	—	—	1.5	—	Sterile
10/11	20	Bloody	Normal	26	4	648	33	395	—	1.6	—	Sterile
10/14	20	Clear	Normal	30	0	121	32	416	—	Trace	—	Sterile
10/19	45	Clear	Normal	40	11	192	32	434	—	Trace	—	Sterile
10/23	25	Clear	Normal	12	4	169	29	—	—	Trace	—	Sterile
10/29	25	Clear	Normal	9	2	++	+	—	—	—	—	Sterile
10/30	45	Clear	Normal	0	0	112	23	407	—	Absent	—	Sterile

The organism did not liquefy gelatin; the result of the indol test was positive, of the methyl red test negative, of the Voges-Proskauer test negative and of the Koser citrate growth test positive. The patient's blood serum did not agglutinate the organism. The bacillus did not kill a mouse. It could not be definitely classified as to type but was thought to be a usually nonpathogenic inhabitant of the intestinal tract belonging to the Bacillus coli anaerogenes group. This conclusion was later corroborated by the bacteriology department of the National Institute of Health of the United States Public Health Service.

Clinical Course: The patient was at once given sulfapyridine orally, a total of 0.8 Gm. daily being administered in six doses. For feedings a mixture of 3 parts of milk to 1 part of water with a 5 per cent preparation of dextrin and maltose was ordered. The infant was closely observed, and daily measurements of the head and chest and ocular funduscopic studies were included in the routine examination. She was irritable for two or three days; Kernig signs were present bilaterally, and nuchal rigidity became manifest. Photophobia was present, and one or two feedings were regurgitated daily. The temperature fluctuated between 102 and 103 F. However, the appearance and behavior were, in general, good and seemed to belie the hopeless outcome usually expected in meningitis caused by coliform organisms. On the fifth day, acrocyanosis was striking and the respirations were deep. The amount of sulfapyridine given was cut to 0.4 Gm. daily. The infant continued to improve, taking her feedings well and gaining weight steadily. Orange juice and percomorph liver oil were added to the diet. However, despite the patient's surprisingly good behavior, the laboratory data did not parallel the clinical course. Examinations of the blood showed persistent leukocytosis and a falling hemoglobin level and red cell count. The cerebrospinal fluid contained no sugar on qualitative test, and its high protein content was out of all proportion to the cell count. Because it was thought that the developing anemia might be an effect of the medication, the dose of sulfapyridine was gradually reduced until the drug was discontinued entirely on September 10, after a two weeks' trial.

Two days later the temperature suddenly rose to 101.6 F.; the infant became markedly pale and her respirations rapid. The pulse rate rose to 216 per minute, and a systolic murmur became audible over the precordium. There was no change in the neurologic status. However, lumbar puncture again showed a fluid with marked pleocytosis, and there were organisms on direct smear. Two successive daily transfusions of 75 cc. of citrated blood were given, and sulfapyridine therapy was reinstituted. During the next few days the infant had moderately severe diarrhea (nine or ten yellowish mucoid stools daily). A mild catarrhal inflammation of the left ear was also observed. Vomiting again became a distressing feature. The fontanel was full, the neck rigid, and the Kernig sign was present bilaterally. The temperature hovered between 101 and 103 F., and the pulse rate was maintained at more than 200 beats per minute.

The diarrhea finally was controlled on a skimmed milk regimen, and after receiving the transfusions and the sulfapyridine the infant once again began to look well. The cell count of the cerebrospinal fluid again dropped, and the result of the Benedict qualitative test for sugar became positive. The temperature remained normal despite a second discontinuation of sulfapyridine therapy, and the growth of the skull did not exceed the normal increment. The weight, which on admission was 6 pounds 11 ounces (3,040 Gm.), had risen to 9 pounds 9 ounces (4,345 Gm.) in forty days. The hemoglobin level had risen to 80 per cent and the red cell count to 3,800,000 per cubic millimeter. Physical examination revealed no abnormalities, and the patient was discharged as improved on October 4.

Second Admission.—Three days after discharge she again became restless and irritable, and for a third time loose stools were passed. The feedings were vomited and the temperature rose to 102 F. When seen again, on October 8, the patient had a bulging anterior fontanel and a distended abdomen. Rehospitalization was advised. Lumbar puncture yielded clear cerebrospinal fluid under normal pressure, with 137 cells per cubic millimeter; a smear was negative and a culture sterile. Again sulfapyridine therapy was instituted. Diarrhea continued for three days. Culture of a specimen of urine revealed the same organism that had previously been found in the blood and the cerebrospinal fluid. Because of the falling hemoglobin level and red cell count two additional blood transfusions were given. Roentgenograms of the chest, the long bones and the skull were normal.

Because of the bacteriuria it was decided to investigate the genitourinary tract for abnormalities. Consequently, on the morning of October 14, 100 cc. of a solution of diodrast N. N. R. (20 cc. of dye in 100 cc. of distilled water) was given subcutaneously, and roentgenograms of the kidneys, which proved to be entirely normal, were made. That noon, while the infant was receiving her first

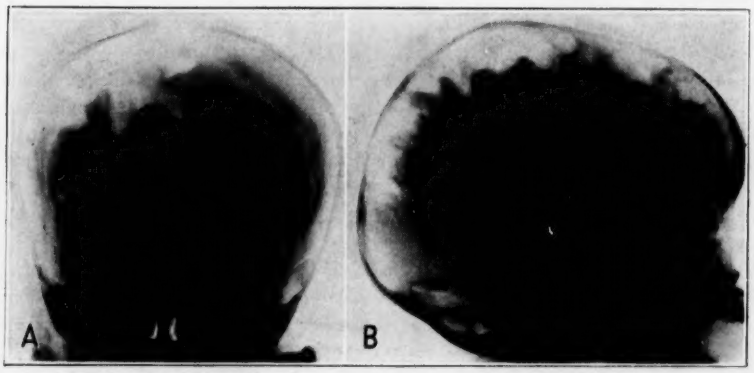

Fig. 1.—Pneumoencephalogram taken Oct. 19, 1939. *A*, anteroposterior view, and *B*, lateral view. The abnormal quantity of air above the left side of the cortex and the irregularity in the sulcus markings were interpreted as indicating atrophy of the left side of the brain.

feeding of the day, she suddenly vomited, and during one hour had two convulsive seizures on the left side, which involved successively the foot, the leg, the arm, the hand and the face. The shrill cry returned, and transient palsies of the sixth nerve on the left and the seventh nerve on the right were observed. Lumbar puncture produced a clear fluid containing 30 cells per cubic millimeter and no sugar on qualitative test. The protein content reached a peak of 648 mg. per hundred cubic centimeters. The infant yawned excessively, and the right pupil was persistently larger than the left. The deep reflexes were exaggerated on the left. The eyegrounds were normal, and the head continued to grow, but not too rapidly. It was thought that the focal seizures and residual neurologic signs referable to the right side of the cortex were more likely due to adhesions or to scarring than to an inflammatory mass such as an abscess, since there was no evidence of increased intracranial pressure.

Three days after the convulsive seizures, on October 17, an electroencephalographic examination was performed, and on October 19 a pneumoencephalographic examination was made (fig. 1). In the latter procedure 45 cc. of cerebrospinal

fluid was removed and replaced with 40 cc. of oxygen. The report was as follows:

"The pneumoencephalograms show poor visualization of the cerebral ventricles. There is, however, evidence of a considerable amount of air above the left side of the cortex, with great irregularity of the sulcus markings. On the right no free air can be seen overlying the plane surface, in all probability as a result of adhesions. The observations are consistent with a diagnosis of atrophy of the left side of the brain."

The procedure was repeated on October 30, and again the ventricular system filled poorly. Air was found throughout the subarachnoid spaces, which were markedly deformed. Large foci of atrophy could be demonstrated, especially superiorly in the posteroparietal region and inferiorly in the right temporal region (fig. 2).

The electroencephalogram was interpreted as follows:

"The most apparent abnormality in the record is the failure of the potentials to gain in amplitude or change observably in position when the infant appeared

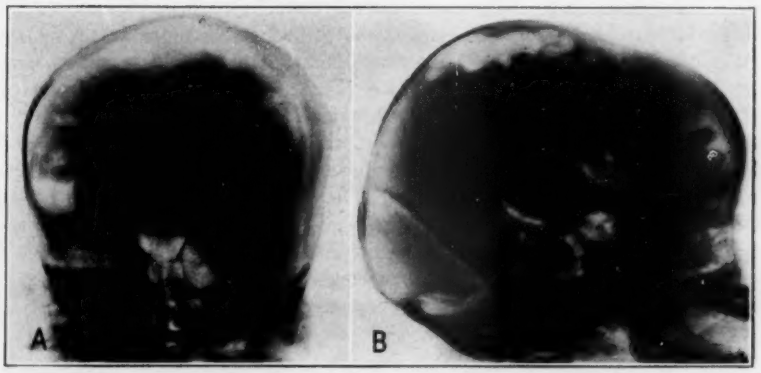

Fig. 2.—Pneumoencephalogram taken Oct. 30, 1930. *A*, anteroposterior view, taken in the prone position, and *B*, lateral view, taken in the erect position. The excess of air in the posteroparietal and temporal regions was interpreted as indicating foci of atrophy of the brain.

to be drowsy or when her eyes were closed and she gave every indication of being asleep. During a few short periods of activity potentials resembling those recorded from patients with petit mal were observed. They appeared when the infant was quiet, as well as when she moved, and were not localized as to region. The impression gained is that there is diffuse electrical abnormality, which is not marked but which may be more outstanding in the occiptal and right temporal areas. The picture also presents evidence for convulsive activity."

The patient had no further convulsions. The temperature remained normal, and the infant again thrived. Feedings were taken well, and the weight curve continued upward. The abnormal neurologic signs, except for pupillary inequality, gradually disappeared. The skull did not increase abnormally in size. It was believed that there was a plastic exudate over the surface of the brain which was preventing its growth and expansion. The abnormalities of the cerebrospinal fluid were thought to be due to pockets of pus deep in the sulci. The opinion was expressed at this time that sulfapyridine was probably acting as a bacteriostatic

agent but that because of the infant's notoriously deficient ability to form antibodies there was a sufficient number of living organisms to produce pleocytosis and occasional qualitative disappearance of sugar. The high total protein content of the cerebrospinal fluid could also be explained by the presence of walled-off small abscesses deep in the sulci.

Medication was gradually eliminated. The infant became bright, alert and playful. The anisocoria remained. From the clinical examination alone the possibility of a favorable outcome and normal mental development began to loom larger.

Results of a psychometric examination performed a week before the second discharge, at the age of 3 months, were reported as follows:

"On the basis of the tests there was no detectable psychometric impairment. The patient accomplished all responses expected of a normal 3 month old infant and many of those not usually attained until the age of 4 months. Her reaction to a mirror image was even precocious. She gazed at her face for a prolonged period, smiled, frowned and so on. There is certainly no correlation at present between the infant's mental capacities (as tested) and the definitely pathologic intracranial condition demonstrated on the pneumoencephalogram."

After her discharge from the hospital the patient returned for follow-up study on May 14, 1940, at the age of 9 months. Her weight was 21 pounds 4 ounces (9,660 Gm.), and she looked well. She had had one cold and had been successfully vaccinated for smallpox and immunized against diphtheria. She had had no further convulsions. She was alert, bright, active and happy. She sat up alone and walked if supported. She reached for and played with objects. She was able to say a few simple single words. The sizes of the head and chest were proportionately normal for a child of her age. The pupils were equal and reacted to light; the fundi were normal. There were no palsies or pathologic reflexes. All observers, including the parents, the psychologist and those who had watched her during her hospital stay agreed that she appeared to be in every sense a normal child. When last heard from, in July 1940, she was progressing well.

COMMENT

Most previous reports on meningitis caused by coliform organisms have taken for granted the ineffectiveness of therapy and the utterly hopeless prognosis and have been concerned with other factors, notably the incidence and the pathogenesis. Details of bacteriologic and pathologic observations, diagnosis and therapy have appeared in a few scattered instances, but for the most part they have not been stressed.

Incidence.—A number of observers have drawn attention to the relative infrequency with which meningitis is due to infection with coliform bacilli. Among the earliest reports is that of Scherer,[1] who in 1895, in a study of 1,500 cases of purulent meningitis in children, found 3 in which the cause was Bacillus coli communis. Holt,[2] in 1911, listed 1 case among 300 cases of acute meningitis in infants and children avail-

1. Scherer, F.: Ein Beitrag zur Aetiologie der Leptomeningitis bei Säuglinger, Jahrb. f. Kinderh. **39**:1, 1895.

2. Holt, L. E.: Observations on Three Hundred Cases of Acute Meningitis in Infants and Young Children, Am. J. Dis. Child. **1**:26 (Jan.) 1911.

able for study and added another from his private practice. Neal,[3] in 1926, also commented on the comparative rarity of meningitis caused by organisms of the colon group. In an analysis of the 1,500 cases of the disease occurring in patients of all ages listed by the Meningitis Division of the Bureau of Laboratories of the Department of Health of the City of New York up to 1924 she found that B. coli was grown in pure culture in only 5, in mixed culture in a sixth. She collected 68 cases from the literature, including 1 of her own. In only 3 of 50 cases of meningitis of all types occurring in patients under 3 months of age was the disease caused by B. coli. On the other hand, reports confining themselves more closely to meningitis of the newborn have pointed out the preponderance of the coliform group as the offending organisms. Barron,[4] in 1918, in perhaps the most exhaustive review of meningitis of the newborn up to that time, emphasized that meningitis was exceedingly rare in the early months of infancy. He was able to tabulate only 42 occurrences in patients up to the age of 5 months; 39 of these patients were under 3 months, and 19, including his own, were newborn infants. However, B. coli was the causative organism in 7 of these 19 cases. Of the cases of meningitis in patients under 3 months of age, this organism was the etiologic agent in 33 per cent. Karplus,[5] in 1927, found that in 12 of 40 cases of meningitis in the newborn, or 30 per cent, the causal organism was B. coli. Cruickshank,[6] in 1930, listed meningitis as the cause of 33 of 800 deaths of newborn infants. Of these 33 fatal cases of meningitis there were 11 in which coliform bacilli were grown in pure culture. Fothergill and Sweet[7] were able to gather reports of 705 cases of meningitis in infants and children during the twelve year period ending in 1933. There were 9 cases in which members of the colon group of bacilli were the causative agent, 8 of which occurred in patients between the ages of 1 and 5 weeks and the ninth in a 10 year old child. In 1936 Craig[8] gave an account of 21 cases of meningitis in newborn infants. In over half B. coli was the causative organism, the remainder being of coccal origin.

3. Neal, J. B.: Meningitis Caused by Bacilli of the Colon Group, Am. J. M. Sc. **172**:740, 1926.

4. Barron, M.: Meningitis in the Newborn and in Early Infancy, Am. J. M. Sc. **156**:358, 1918.

5. Karplus, D.: Die Meningitis des Neugeborenen, Wien. klin. Wchnschr. **40**: 250, 1927.

6. Cruickshank, J. N.: Child Life Investigations: The Causes of Neo-Natal Death, Medical Research Council, Special Report Series, no. 145, London, His Majesty's Stationery Office, 1930.

7. Fothergill, L. D., and Sweet, L. K.: Meningitis in Infants and Children, with Special Reference to Age Incidence and Bacteriologic Diagnosis, J. Pediat. **2**:696, 1933.

8. Craig, W. S.: Meningitis in the Newborn, Arch. Dis. Childhood **11**:171, 1936.

There are no conflicting views in these reports. In summary, they point out that: (1) meningitis is much less common in the early months of infancy than in childhood; (2) the coliform organisms are rare offenders when one includes all the meningitides in infancy and childhood; (3) during the period up to 3 months of age, however, especially in newborn infants, the coliform bacilli are the commonest cause of meningitis.

In addition to these reports of larger numbers of cases, there are revealing and interesting papers dealing either with smaller groups or with individual cases of meningitis caused by coliform organisms. These include the presentations of Hinsdale,[9] Kovalevsky and Moro,[10] Goldreich,[11] Noeggerath,[12] Forbes,[13] Smith and Woodforde,[14] Pearson,[15] Koplik,[16] Frank,[17] Lindberg,[18] Cooke and Bell,[19] Neff,[20] Mulhern and Seelye,[21] Vonderahe and Baurichter,[22] Gibbens,[23] Athenstaedt,[24] Pounders,[24a] Eckstein,[24b] Ravid,[24c] Crockford [24d] and Thompson and Quinn.[25]

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9. Hinsdale, G.: Purulent Encephalitis and Cerebral Abscess in the New-Born Due to Infection Through the Umbilicus, Am. J. M. Sc. **118**:280, 1899.

10. Kovalevsky, O. V., and Moro, E.: Ueber zwei Fälle von Coli-Septicaemie bei Neugeborenen, Jahrb. f. Kinderh. **55**:220, 1902.

11. Goldreich, L.: Meningitis im Neugeborenen, Jahrb. f. Kinderh. **56**:808, 1902.

12. Noeggerath, C. T.: Bacillus coli immobilis capsulatus (Wilde) bei einem Fall von eitriger Meningitis cerebrospinalis, München. med. Wchnschr. **54**:617, 1907.

13. Forbes, J. G.: The Pathology of the Cerebro-Spinal Fluid Derived from Lumbar Puncture, Quart. J. Med. **1**:109, 1907.

14. Smith, E. B., and Woodforde, A. W. G.: Two Unusual Forms of Meningitis Occurring in Infancy, Lancet **2**:236, 1912.

15. Pearson, G. H.: A Case of Meningitis in Which the Bacillus Coli-Communis Was Obtained from the Cerebrospinal Fluid, Lancet **1**:722, 1912.

16. Koplik, H.: Meningitis in the Newborn and in Infants Under Three Months of Age, Arch. Pediat. **33**:481, 1916.

17. Frank, E. S.: Parakolimeningitis, Nederl. tijdschr. v. geneesk. **1**:888, 1916.

18. Lindberg, G.: Meningealblutung und eitrige Meningitis im frühen Säuglingsalter, Jahrb. f. Kinderh. **86**:363, 1917.

19. Cooke, J. V., and Bell, H. H.: The Incidence of Meningitis in Early Infancy with a Description of Two Cases Due to Unusual Organisms, Am. J. Dis. Child. **24**:387 (Nov.) 1922.

20. Neff, F. C., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 7, p. 555.

21. Mulhern, M. E., and Seelye, W. B.: A Case of Meningitis in a Newborn Infant Due to a Slow Lactose-Fermenting Organism Belonging to the Colon Bacillus Group, J. Lab. & Clin. Med. **21**:793, 1936.

22. Vonderahe, A. R., and Baurichter, F. X.: Bacillus Coli Meningitis, Ohio State M. J. **27**:370, 1931.

(Footnotes continued on next page)

Pathogenesis.—Because meningitis due to B. coli or to related organisms appears to be distinctive and peculiar to newborn children and to infants in the first two or three months of life, and seems to become relatively rare in older infants and children, many authors have ventured to speculate about the pathogenesis of the disease. As early as 1895 Scherer [1] expressed the belief that a higher incidence of meningitis in infancy caused by B. coli occurred in hospitals during periods of overcrowding. He expressed the opinion that infection in his own patients arose from bathing infants in contaminated water. This resulted in otitis media, which in turn led to purulent meningitis. Vonderahe and Baurichter [22] had reported a case in a child and Thompson and Quinn [25] a case in an adult in which it was thought that an almost identical sequence of events had led to the development of the disease. Both patients had swum in contaminated water, and in the former case the course of events, in order, had been otitis media, mastoiditis and meningitis; in the latter it was presumed that the virulent bacteria had gained access to the nasal passages and thence to the meninges. Segiet,[26] in 1939, confirmed Scherer's [1] original views by the observations in 3 of his own cases. Goldreich [11] invoked a variation of the theory of aspiration. In his case the fetus was thought to have sucked contaminated amniotic fluid into the respiratory passages. This resulted in purulent bronchitis and allowed transmission of the infecting organism from the lungs to the brain by way of the blood stream. Several writers have implicated the patient's genitourinary tract as the primary site of infection. Kovalevsky and Moro,[10] Allard,[27] Holt,[2] Neal [3] and Koplik [16] have cited instances in which this site was the source of the infection. Koplik reported a case in which colipyelitis followed infection of a circumcision wound. Athenstaedt [24] described an instance in which colipyelitis was present in the mother and was probably transmitted transplacentally to

23. Gibbens, J.: B-Coli Meningitis in the Newborn, Lancet **1**:1298, 1932.

24. Athenstaedt, F.: Colisepsis des Neugeborenen bei Pyelitis gravidarum der Mutter, Zentralbl. f. Gynäk. **57**:2302, 1933.

24a. Pounders, C. M.: Meningitis in the Newborn, J. Pediat. **4**:752, 1934.

24b. Eckstein, A., in von Pfaundler, M., and Schlossmann, A.: Diseases of Children, translated from the fourth German edition by M. G. Peterman and others, Philadelphia, J. B. Lippincott Company, 1935, vol. 5, p. 414.

24c. Ravid, J. M.: Meningococcic and Nonmeningococcic Meningitis in the Newborn and in Young Infants, Am. J. Dis. Child. **49**:1282 (May) 1935.

24d. Crockford, A. L.: A Case of B-Coli Meningitis, Brit. M. J. **1**:1101, 1938.

25. Thompson, H. F., and Quinn, R. P.: Meningitis Caused by Bacillus Coli, J. Iowa M. Soc. **29**:611, 1939.

26. Segiet, W.: Zur Pathogenese der sogenannten Coli-Meningitis der Neugeborenen, Frankfurt. Ztschr. f. Path. **53**:208, 1939.

27. Allard, E.: Die Lumbalpunktion, Ergebn. d. inn. Med. u. Kinderh. **3**:100, 1909.

the fetus. Barron [4] cited an example in which the infection probably began in the infant's mouth as a result of traumatization by the finger of the accoucheur. Craig [8] stressed morbid conditions of the skin and surface mucous membranes as primary foci of infection. Forbes [13] presented a case of meningitis secondary to spina bifida. In Pearson's [15] patient, a 3 month old girl, the left middle ear was full of pus, but no thrombosed vein or caries of bone was found post mortem. Cooke and Bell [19] expressed the belief that the condition in their cases should be termed "primary meningitis," since the origin of the infection was obscure. They thought it natural to assume that the organisms were derived from the intestinal tract and reached the meninges through the blood. To support their hypothesis they submitted evidence of (1) the greater permeability of the intestinal mucosa in early infancy, (2) the decreased resistance of young infants to bacterial infection associated with defective antibody formation and (3) the influence of digestive disturbance and malnutrition in predisposing to infection. Karplus [5] and Ravid [24c] expressed agreement with this theory, and the latter elaborated on it. He indicated that the normal agglutinin for B. coli is found in a much higher quantity in the blood of adults than in that of young children and, what is most significant, that in the blood of fetuses and of newborn infants this agglutinin is absent. Coupled with this are the observed phenomena of increased permeability of the gastrointestinal mucosa of extremely young infants to bacteria and foreign protein. Therefore, when organisms such as B. coli accidentally and suddenly gain access to the body of a newborn infant they meet with no resistance because of the lack of acquired immunity. It is surmised that infection spreads through the blood with ultimate selective localization in the pia-arachnoid. Pounders,[24a] too, expressed the belief that this was the mode of entry of the organism and added that perhaps intracranial birth injury made the brain a point of low resistance where the organism could lodge. Kovalevsky and Moro,[10] Karplus [5] and Athenstaedt [24] expressed the belief that the meningitis was part of a primary sepsis. The latter suggested that the umbilicus, the gastrointestinal tract, the urinary passages, the skin, the mucous membranes or the mother, by way of the placenta, could serve as primary sources of infection. The observations in Anspach's [30] 6 cases seem to confirm the probability that some of the sites referred to did serve as primary foci. In 3 there had been gastrointestinal disturbances, while cerebral injury, otitis media and colinephritis in the mother accounted for the remainder. Cruickshank's [6]

28. Footnote deleted.

29. Footnote deleted.

30. Anspach, M. K.: Die weitere Schicksal der in der Leipziger Kinderklinik in der Jahren 1924 bis 1934 beobachteten Fälle von Meningitis purulenta, Monatschr. f. Kinderh. **66**:364, 1936.

postmortem studies gave added corroboration to the concept of general sepsis. It remained for Fothergill and Sweet,[7] however, to demonstrate that during life bacteremia was almost universally present, the same organism being isolated from the blood as from the cerebrospinal fluid. It is quite probable that there is no one theory of pathogenesis to explain correctly the mechanism in all cases.

In relating our own experience we find that the illness began with diarrhea and that each relapse was heralded by a similar episode of gastrointestinal disturbance. Moreover, colibacteremia was present on admission, and subsequently colibacilluria, without any grossly pathologic genitourinary condition being demonstrable. The organisms recovered were identical with those found in the cerebrospinal fluid. Since the mother was in apparent good health throughout her pregnancy, one might predicate an external source for the infection. The possibility that the organisms were present in the unskilfully produced milk of local supply which was fed the infant presents itself. In reconstructing the picture, the events, in order, seem to have been gastroenteritis, invasion of the blood stream by large numbers of the organisms through the intestinal mucosa and, finally, localization in the meninges. The bacteriuria may be likened to that occurring in patients with typhoid fever and does not necessarily mean renal involvement. Unfortunately, the stools were not cultured, but they probably would have yielded the suspected organism had this procedure been carried out.

Bacteriology.—In analyzing some of the available reports on the bacteriology of meningitis, one is struck by the lack of unanimity not only in the interpretation of the role of the organism in the pathogenesis of the disease but in the classification of the various types to which significance is attached. For example, Cruickshank[6] has raised the question as to whether the presence of coliform organisms at autopsy in the majority of cases he described might not have been due to agonal or postmortem invasion of tissues. Certainly, the finding of bacteremia during life and early in the course of the disease should dispose of this doubt. On the other hand, Smith and Woodforde[14] would like to classify colimeningitis into two types, serous and suppurative, and answering the question as to whether the organism in the first group is not an accidental invader becomes more difficult. In fact, some observers would take issue with such a diagnosis as "coliform serous meningitis." Cooke and Bell[19] have suggested the possibility that certain members of the colon group of bacilli may be particularly associated with meningitis in infancy but that this could be established only by comparison of the descriptions of the cultures isolated. They added that because of the multiplicity of types and the differences in classification of this group considerable detail in description of strains isolated from such patients would be of value.

A somewhat more general view in nomenclature has been taken by Breed and Norton.[31] In 1937, these writers pointed out that the aerobic, non-spore-forming, lactose-fermenting bacteria appear under a variety of names in the literature, e. g., "B. coli," "E. coli," "colon," "colon-aerogenes," "coli-aerogenes," "Escherichia-Aerobacter" and "coliform." These terms have been used to signify the group of organisms defined as including all aerobic and facultative anaerobic, gram-negative, non-sporing bacilli which ferment lactose with the formation of gas. The authors suggested the introduction of the term "coliform" to designate the whole group. On the other hand, in a recent publication, Stuart, Mickle and Bowman [32] took issue with the encompassing classification of Breed and Norton.[31] They went more into detail and set aside four subgroups of aberrant coliform organisms. These include strains differing from typical coliform organisms with respect to their fermentation of lactose (producing less than 20 per cent of gas in forty-eight hours at 37 C.). The fourth of the subgroups they call anaerogenic coliform organisms. These are aberrant coliform organisms which produce acid but no gas from the fermentation of lactose.

Zinsser and Bayne-Jones [33] noted that in 1920 a committee of the Society of American Bacteriologists grouped under the generic name "Bacterium" all the aerobic non-spore-forming rods in the intestine. They stated: "The subdivisions of the group may be indicated as follows: I. Colon-aerogenes group. This includes *Bacterium coli, Bacterium aerogenes* and related organisms. It has affinities with the Friedländer bacilli . . . II. The paratyphoid group . . . III. The typhoid group . . . IV. The dysentery bacilli . . . The most important differential characteristics are fermentative actions upon carbohydrate media, action on gelatin, and agglutinating reactions in immune sera." They also remarked that infection in man takes place because of an unusual temporary reduction of resistance of the host and that rarely, in newborn infants, a primary invasion of the circulation by the bacilli may occur.

In dealing with colon bacilli the bacteriologist is confronted with variations which may be due to several causes. The organisms gain and lose fermentative capacities in ways that are sometimes unpredictable and exhibit dissociative variability into smooth, rough, mucoid, motile and nonmotile, aerogenic and nonaerogenic and antigenically different forms. The general characteristics of the group of colon

31. Breed, R. S., and Norton, J. F.: Nomenclature for the Colon Group, Am. J. Pub. Health **27**:560, 1937.

32. Stuart, C. A.; Mickle, F. M., and Borman, E. K.: Suggested Grouping of Slow Lactose Fermenting Coliform Organisms, Am. J. Pub. Health **30**:499, 1940

33. Zinsser, H., and Bayne-Jones, S.: A Textbook of Bacteriology, New York, D. Appleton-Century Company, Inc., 1939, vol. 8, p. 489.

bacilli are defined by the American Public Health Association Committee on Standard Methods of Water Analysis[34] as: "Gram-negative rods, aerobic, facultatively anaerobic, growth on gelatin without liquefaction, fermentation of dextrose and *lactose* with gas formation." Other differential tests include (1) the methyl red test (the reaction of Bact. aerogenes is negative, of Bact. coli positive); (2) the Voges-Proskauer reaction (the reaction of Bact. aerogenes is positive, of Bact. coli negative); (3) growth on Koser's sodium citrate medium (Bact. aerogenes is able to grow, Bact. coli is not).

In the light of these observations it is possible to reconcile some of the atypical reactions of the organisms listed in table 2, which were reported by others and by us, with those of types showing standard growth behavior.

From this table it is seen that the organism isolated from our patient is a fermenter of lactose which also attacks most of the other sugars, with the exception of saccharose. The unusual feature is the lack of vigor in the growth, expressed by the failure to form gas. Its action on methyl red and sodium citrate mediums is characteristic of Bact. aerogenes, while in the Voges-Proskauer reaction it resembles B. coli. Hence the classification of the organism as Bacterium coli aerogenes by both of the laboratory staffs that studied it. The name "aerogenes" applied to an organism which does not produce gas seems to be a contradiction of terms. We therefore felt that perhaps the more appropriate name would be "Bacterium coli anaerogenes" or "anaerogenic coliform bacterium," as was previously suggested.[32]

Pathology.—The most complete description of the pathologic observations in this series was recorded by Craig.[8] This author found that the extent of the inflammatory exudate varied. In some places there was a thin deposit along the lines of the meningeal vessels; in others a thick exudate was limited to the base of the brain and the lateral fissures and in a few a massive purulent deposit extended uniformly from the vertex to the base and involved the surfaces of the midbrain and the cerebellum. Intense generalized congestion of the meninges was characteristic even when the inflammatory deposit was strictly localized. The choroid plexus was covered in a number of instances, and the ventricular wall in a few instances, with exudate similar to that on the surface of the brain. Abundant exudate was sometimes accompanied by flattening of the cerebral convolutions over the cortex. Hemorrhage away from thrombosed vessels was occasionally present. Neal[3] noted that in infants under 6 months of age with meningitis subacute arachnoiditis is particularly prone to develop and that if the inflammation continues the foramen of Magendie is completely cut off.

34. Zinsser and Bayne-Jones,[33] p. 495.

TABLE 2.—*Data on Some of the Organisms Recovered from Patients with Meningitis Caused by Coliform Organisms*

Author	Fermentation of					Indol	Growth on Methyl Red Medium	Voges-Proskauer Reaction	Growth on Koser's Sodium Citrate Medium	Liquefaction of Gelatin	Motility	Animal Inoculation	Agglutination of Own Serum	Age of Patient	Outcome of Infection	Author's Comments
	Dextrose	Lactose	Maltose	Mannitol	Saccharose											
1. Hinsdale [9]	Acid; gas	Acid; gas	Acid; gas	.....	Acid; gas	+	..	..	..	0	0	Guinea pig died in 12 hr.	..	4 days	Died	Classed as B. coli immobilis
2. Smith and Woodforde [14]	Acid; gas	Acid; gas	.....	Acid; gas	0	+	..	..	..	0	..	..	..	5 mo.	Died	Classed as B. coli communis
3. Barron [4]	Acid; gas	Acid; gas in 4 days	Acid; gas	Acid; gas	0	+	..	..	..	0	+	..	..	..	Died	
4. Cooke and Bell [19] (case 1)	Acid; gas	Acid; delayed	Acid; gas	Acid; gas	Acid; gas	+	+	0	..	0	+	..	1 to 80	10 wk.	Died	
5. Cooke and Bell [19] (case 2)	Small quantities of acid; no gas	Small quantities of acid; no gas	Small quantities of acid; no gas	Small quantities of acid; no gas	Small quantities of acid; no gas	+ in small amount	..	..	..	+	0	Guinea pig and rabbit survived	0	4 wk.	Died	Growth elastic; capsule produced; did not attack sugars energetically; classed as Bacterium elasticum
6. Pounders [24a]	Acid	Acid	.....	Acid	Acid	..	..	..	..	..	..	Guinea pig and rabbit survived	1 to 300	5 wk.	Died	Member of colon group but not identical with B. coli; belongs to group of saprophyte ordinarily present in gastrointestinal tract
7. Rauch and Krinsky	Acid	Acid	Acid	Acid	0	+	0	0	+	0	0	Mouse survived	0	3 wk.	Recovered	Organism could not be classified; probably a usually nonpathogenic inhabitant of intestinal tract; classed as Bact. coli aerogenes

These adhesions and blockage of the circulation of the cerebrospinal fluid lead to hydrocephalus or pyocephalus. Indeed death or recovery with sequelae were most commonly associated with the latter development. This is amply borne out in the reports of Holt,[2] Smith and Woodforde,[14] Lindberg,[18] Koplik,[16] Neff,[20] Fothergill and Sweet,[7] Ravid [24c] and Anspach.[30] The patient reported on by Hinsdale [9] had an abscess of the frontal lobe, an unusual complication.

Diagnosis.—The diagnosis of meningitis in early infancy is notoriously difficult, since no special pathognomonic signs are present. Ravid [28] has singled out the signs and symptoms that are highly suggestive of meningitis in infancy. These include hyperesthesia, irritability, somnolence, incessant crying, convulsions, tenseness or bulging of the fontanel, distention of the veins of the neck and gastrointestinal disturbances of any sort. Craig [8] has added that the signs of ocular incoordination and nystagmus, associated with an expression of fear or with restless movements of the head, are of particular value. Both agreed that signs of intracranial disturbance occurring after the first week of life should always suggest the possibility of meningitis and that the most reliable diagnostic measure, namely, spinal puncture, should be resorted to. We should like to add, parenthetically, that the possibility of carrying out this procedure on any patient with a puzzling syndrome in early infancy ought also to be entertained.

Prognosis.—Athenstaedt,[24] Pounders,[24a] Craig,[8] Kutscher [35] and Ravid [24c] have commented on the hopelessness of the prognosis in colimeningitis. The last author, however, forecast in 1935, that the outlook might change with the discovery of newer methods of treatment, a prediction that is already being borne out. The course of the disease and the eventual outcome had heretofore been closely linked with the pathologic changes. As has been remarked, death was most frequently associated with the development of hydrocephalus (or pyocephalus). Reports of recovery, partial or complete, are scattered and lacking in detail. Forbes,[13] in 1907, mentioned the case of a patient with spina bifida in which B. coli was grown in the spinal fluid; the patient recovered. One of Holt's [2] patients recovered from the acute symptoms of meningitis, but hydrocephalus developed. Smith and Woodforde [14] cited Concetti's [36] report of 2 cases of serous meningitis in which recovery occurred, but these cases are hardly acceptable as unequivocal instances of colimeningitis. In the same category falls the occasionally cited case of a 4½ week old infant with B. coli septicemia and cerebral symptoms which was reported by Gibbens.[23] Lumbar puncture yielded normal

35. Kutscher, G. W.: Alkaligenes Bookeri Meningitis: Review of the Literature on Gram-Negative Bacillus Meningitis, Arch. Pediat. **54**:610, 1937.

36. Concetti, cited by Smith and Woodforde.[14]

cerebrospinal fluid, and the author himself granted that he could not prove that this was a case of B. coli meningitis. Frank [17] reported on a 6 month old infant who had recovered from paracolon meningitis of six days' duration. Koplik's [16] 8 day old patient lived for sixteen months after the acute symptoms appeared; hydrocephalus developed and the child died of asthenia and necrosis of both eyes. Neff's [20] patient survived, with sequelae of hydrocephalus, mental and physical retardation and strabismus. Neal [3] also cited the case of a 5 week old infant in whom hydrocephalus developed and who died nearly a year after recovery from the acute symptoms of meningitis caused by B. coli. Eckstein [24b] described the cure of a 6 week old infant, and Thompson and Quinn,[25] in 1939, presented an instance of recovery in an adult. Anspach,[30] in an analysis of the subsequent fate of patients with all types of purulent meningitis over ten years' observation, pointed out that if there was recovery from the acute symptoms the outcome might be expected to be the same for meningitis caused by B. coli as for other types. If the recovery was not complete hydrocephalus, iridochoroiditis and abscess of the vitreous humor might result. Some of the conditions noted on follow-up study of the patients were headache, easy excitability, restlessness, paralysis, spasms, blindness, deafness, imbecility and hydrocephalus.

Therapy.—Notations on therapy are, as expected, scanty. Smith and Woodforde,[14] in 1912, reported on the use of a vaccine made from the organism isolated from the cerebrospinal fluid. Their infant patient seemed to improve for a few days before death. Cooke and Bell,[19] in 1922, tried the intraventricular injection of the patient's serum, without effect. Athenstaedt,[24] in 1933, suggested the use of vaccine or the mother's blood. Eckstein's [24b] patient recovered after the intraventricular administration of methenamine U. S. P. Recovery of the adult patient described by Thompson and Quinn [25] occurred after the use of oral administrations of sulfapyridine, blood transfusions and repeated lumbar puncture. This, substantially, is also the routine that we independently employed. Incidentally, it was also the therapeutic regimen instituted by Katsampes and Bradford [38] in their recent report on a month old infant who recovered from Salmonella (Panama) meningitis. It is interesting to note that this patient had a relapse, as did ours, before complete recovery occurred. Today, with the almost unrestricted trial of sulfonamide chemotherapeusis in nearly every type of seemingly hopeless infection, this manner of approach to the problem of the treatment of colimeningitis need hardly be urged.

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37. Footnote deleted.

38. Katsampes, C. P., and Bradford, W. L.: Recovery from Salmonella (Panama) Meningitis in an Infant Treated with Sulfapyridine, J. Pediat. **16:79**, 1940.

Are we justified in saying that our patient has completely recovered? To be conservative we should admit that this question will not be answered satisfactorily for another five or six years, when the child will attain school age. Her present status reveals that she has gone for almost a year without the development of the most dreaded of sequelae, hydrocephalus or involvement of the sensory organs. On examination at this time (July 1940), we regard her as mentally and physically normal. To be more certain, of course, pneumoencephalographic studies should be repeated. However, we see no real indication at present for carrying out this not entirely innocuous procedure. Furthermore, as Brines and Lord [39] have shown, this procedure may not be necessary. These authors have decried the universal reliance on the encephalogram alone in making a diagnosis and in formulating a prognosis, especially in children. They pointed out that after an initial insult to the brain the lesion need not remain static or become progressive. They called attention to the fact that, in children at least, actual growth of the tissue of the brain takes place and that the prediction of the child's mental adequacy must depend on the future rate of development. They described 6 patients, observed over ten years, for whom an unfavorable prognosis was given, based chiefly on encephalographic data, and who subsequently had both normal mental developments and normal encephalograms. They concluded that serious errors can result in predicting the subsequent mental age of children less than 3 years old from the interpretation of an encephalogram unsupported by other means of estimating the mental status of a given patient. They suggested that the encephalographic standards for infancy are relatively unreliable and that more knowledge is needed about the resumption of growth and development after disease or cerebral injury. They warned that a single encephalogram is not adequate for the formation of a prognosis.

In our own case, on the basis of the present clinical observations, we feel justified in assuming by analogy that the cortical insult, as judged by the convulsive seizures, pneumoencephalograms and electroencephalograms, was transient. We have reason to believe that the purulent exudate, which prevented the expansion of the brain and which was responsible for an encephalogram which simulated those taken of patients with cortical atrophy, was completely absorbed and that the brain resumed its normal growth, development and function.

SUMMARY

A case of meningitis in a 3 week old infant caused by Bact. coli anaerogenes (anaerogenic coliform organism), with temporary cortical

39. Brines, J. K., and Lord, E.: Place of Encephalography in Prognosis in Childhood, J. Pediat. **15**:836 (Dec.) 1939.

insult and recovery is reported. The presence of colisepticemia and bacteriuria is pointed out, and interesting results of pneumoencephalographic and electroencephalographic examinations, demonstrating cortical changes, are described. The use of oral administration of sulfapyridine, blood transfusions and repeated lumbar puncture is recommended for patients with this type of meningitis.

A review of the literature, with reference to the incidence, pathogenesis, bacteriology, pathology, diagnosis, prognosis and treatment of meningitis caused by "coliform" organisms is given.

Caution in relying on the encephalogram alone in formulating a prognosis is echoed.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

INACTIVATION OF EPIDEMIC INFLUENZA VIRUS BY NASAL SECRETIONS OF HUMAN INDIVIDUALS. THOMAS FRANCIS JR., J. Bact. **39**:54 (Jan.) 1940.

Because there are definite indications that immunity to infection with epidemic influenza virus is not entirely explained by the presence or absence of neutralizing antibodies in the blood, the author began to search for other mechanisms which might be effective in the prevention of infection. The nasal secretions of human subjects were tested for their capacity to inhibit the infectivity of the virus. The material was ground with an abrasive and then centrifuged. The supernatant fluid was then mixed with suspensions of influenza virus, and the mixture was injected intranasally into mice. Of 25 samples tested, 7 failed to neutralize approximately 1,000 fatal doses; 8 gave partial neutralization, while 10 gave complete or almost complete neutralization. The inactivating effect of the secretions apparently does not parallel the titer of humoral antibodies, nor is it related to the bacterial flora.

STOESSER, Minneapolis.

EFFECT OF SULFANILAMIDE AND TRYPAFLAVIN ON CULTURES OF LEISHMANIA TROPICA. H. A. SENEKJI, J. Infect. Dis. **66**:111 (March-April) 1940.

"Leishmania tropica grows in a medium containing sulfanilamide. The inhibitory effect of sulfanilamide on Leishmania tropica is slight, even in the presence of the whole blood. The toxic action on the leptomonads is direct and phagocytosis does not play any role.

"Trypaflavin is highly toxic to Leishmania causing immediate lysis of the leptomonads."

AUTHOR'S SUMMARY.

p_H STABILITY OF THE VIRUS OF EQUINE ENCEPHALOMYELITIS (EASTERN STRAIN) UNDER VARIOUS CONDITIONS. H. FINKELSTEIN, W. MARX, D. BEARD and J. W. BEARD, J. Infect. Dis. **66**:117 (March-April) 1940.

"Infectivity of purified virus diminished rapidly in solutions above p_H 10 and slowly in the acid ranges to about p_H 2.

"Crude chick embryo virus suspensions and suspensions of purified virus to which extracts of non-infected chick embryo tissue had been added showed a similar range of maximum stability between p_H 7 and 10. In addition, a second range of relative stability was exhibited between p_H 3 and 5. Between these acid and alkaline ranges, a region of relatively rapid inactivation was seen in the neighborhood of p_H 5.5. Outside of this range near 5.5, the virus was somewhat more stable in the presence of chick embryo tissue extracts than in the purified state.

"The results might be due to an enzyme, though the nature of the factor and the mode of its action have not yet been determined."

TOOMEY, Cleveland.

Metabolism; Infant Feeding; Milk and Other Foods

COMPOSITION OF SOME COMMON FOODS WITH RESPECT TO THE CARBOHYDRATE CONTENT. THORNE M. CARPENTER, J. Nutrition **19**:415 (May) 1940.

Carpenter analyzed twenty common foods with special reference to their content of reducing sugars, hydrolyzable sugars, starch and cellulose. Determinations of the water, protein, fat and ash content and of the heats of combustion were also made. (See table 1 in the original article.)

FREDEEN, Kansas City, Mo.

THE COMBUSTION OF CARBOHYDRATES IN MAN AFTER INGESTION OF COMMON FOODS. THORNE M. CARPENTER, J. Nutrition **19**:423 (May) 1940.

Carpenter found that increases in the combustion of carbohydrates during the three hours following the ingestion of food were greater if the amounts of reducing and hydrolyzable sugars were greater and that the increases became less the greater the amounts of starch or fat in the foods. FREDEEN, Kansas City, Mo.

WHEAT AS A DIETARY SOURCE OF IRON. ALFRED H. FREE and FRANKLIN C. BING, J. Nutrition **19**:449 (May) 1940.

These investigators found that the iron content of eleven samples of American-grown wheat varied from 2.9 to 4.87 mg. per hundred grams; the average content was 3.94 mg. The ionogenic (also called available or inorganic) iron ranged from 73 to 88 per cent. FREDEEN, Kansas City, Mo.

CARBOHYDRATE VALUES OF FRUITS AND VEGETABLES. R. D. WILLIAMS, L. WICKS, H. R. BIERMAN and W. H. OLMSTED, J. Nutrition **19**:593 (June) 1940.

These St. Louis investigators have found that the accepted values for available carbohydrate of the American fruits and vegetables are too high and suggest that there should be a complete reanalysis of both available and unavailable carbohydrates of these foods.

Four interesting tables accompany the original article.

FREDEEN, Kansas City, Mo.

THE DIET OF ADOLESCENT GIRLS WITH SPECIAL REFERENCE TO NUTRITIONAL STATE AND DENTAL CARIES. LEONA M. BAYER, J. Pediat. **16**:56 (Jan.) 1940.

Data dealing with dietary habits, nutritional status and dental caries, collected during a study of 80 normal adolescent girls examined at the ages of 11.5, 13.5 and 17.5 years, are presented. The diets were generally poor, containing on the average only about two thirds of the recommended essentials. The greatest deficiency was in vegetables, fruits, milk and whole cereals. The impression given by the menus of the group was that the deficiency in nutritionally desirable foods was largely made up by starches and sweets. Half the group were judged as having optimum weight. These girls were shown to have a diet which from the standpoint of nutritional adequacy was slightly superior to that of girls who were overweight and underweight. No statistical relation between poor teeth and poor diet could be demonstrated for this group. It was felt that probably no diets were good enough consistently to exert a protective influence against dental caries.

FROM AUTHOR'S SUMMARY.

THE BASAL METABOLISM OF OBESE CHILDREN. NATHAN B. TALBOT and J. WORCESTER, J. Pediat. **16**:146 (Feb.) 1940.

The basal metabolic rates of a group of obese children presenting no evidence of endocrine disorder were studied with the use of the weight standard, height standard and creatinine standard. The creatinine standard makes it possible to estimate the rate of heat production of the active protoplasmic mass by determining the creatinine output in the urine per twenty-four hours. The results of the determinations showed the average rate obtained by referring to the creatinine standard to be + 14 per cent. This seemed to indicate that the active protoplasmic mass produced heat at an accelerated rate. The height standard gave results (average + 22 per cent) comparable to those obtained from the creatinine standard. An average metabolic rate of — 4.1 per cent was observed when total calories were referred to weight standard. This was taken to mean that these

children produced slightly less than the average amount of heat for their total mass. Apparently the heat-producing tissues had been stimulated to produce more heat in order that the energy requirements of the body as a whole (represented by weight) might be met. The height of these children averaged 3 inches (7.62 cm.) above the mean height of normal children of the same age, and their skeletal age was found to be either average normal or slightly advanced. From these studies the authors conclude that fat boys and girls of the constitution described are not necessarily suffering from a deficiency of anterior pituitary or thyroid hormones.

RAUH, Cincinnati.

THE INTRAVENOUS DEXTROSE TOLERANCE TEST. R. E. TUNBRIDGE and E. C. ALLIBONE, Quart. J. Med. **9**:11 (Jan.) 1940.

A standard intravenous dextrose tolerance test is described in which 27.6 Gm. of dextrose is injected intravenously in three minutes.

The authors performed 132 tests, 40 on healthy medical students and 92 on patients in the hospital.

In healthy young men the level of blood sugar returned to the preinjection level within sixty minutes. The response was altered by age, infection, disease, diet and the amount of dextrose injected and also by insulin, but not by the normal variations in weight or by the use of physiologic solution of sodium chloride instead of water as a solvent for the dextrose. Complications directly attributable to the injection of the dextrose solution occurred in 15 instances.

BRADFORD, Rochester, N. Y.

SOME ASPECTS OF THE MALNUTRITION PROBLEM. J. P. MCGOWAN, Edinburgh M. J. **47**:425 (June) 1940.

This more or less sociopolitical aspect of the nutrition and nutriment problem of the general population deals only briefly with childhood. Generally there is no procedure for separating the amount of undernutrition due to faulty nutriment from that caused by heredity and environment. The writer does not underestimate the value of careful clinical investigation by experts, but he regards as valueless the "extensive, hurried, superficial inquiries conducted on large numbers by amateurs." Much time, money and energy are wasted in observations on groups of children as regards the effect of supplementary feeding. Many environmental factors, material, psychologic and ethical, as well as latent disease (such as tuberculosis) must be included in a survey of nutrition to make it worth while.

NEFF, Kansas City, Mo.

THE USE OF BUTTERMILK IN ACUTE DISTURBANCES OF NUTRITION OF INFANTS. E. TATAFIORE, Lattante **11**:45 (Feb.) 1940.

Tatafiore has been treating severe acute diarrhea in infants by (1) a fasting period of twelve hours, followed by (2) a diet of buttermilk and cereal and (after improvement is manifest) by (3) mother's milk. Case reports are given on 63 patients, with 39 of whom satisfactory results were obtained; there were usually maintenance of body weight, infrequent stools and disappearance of the toxic symptoms after the buttermilk feeding was started.

HIGGINS, Boston.

WEANING. HERMILO CASTANEDA, Rev. mex. de puericult. **8**:357 (July) 1938.

The author suggests the weaning of babies at 6 months because at this age babies are getting their first teeth; because in Mexico the mothers do not have enough milk after this time to prevent malnutrition; because the resistance of the child is increased by supplementary feedings, and because the infants do better

in general. Some nursing can be carried on until the age of 1 year or 15 months. He suggests various milk and sugar formulas and the addition of cereals and vegetables.

HERRON, Oak Ridge, La.

BLOOD SUGAR CURVES IN CARBBOHYDRATE, FAT, AND PROTEIN FUNCTION TESTS AFTER ADMINISTRATION OF CARBOHYDRATE, FAT AND PROTEIN. PAUL GEYER, Jahrb. f. Kinderh. **149**:121 (May) 1937.

A most important finding was that assimilation is considerably affected by previous feedings, sometimes given many hours before.

The differences in the blood sugar values after the use of dextrose alone, given orally and intravenously, and after the use of fat and protein are given. Numerous examples of the blood sugar curves under various conditions are shown graphically.

LANDAU, Hannibal, Mo.

Vitamins; Avitaminoses

PELLAGRA IN INFANCY AND CHILDHOOD. TOM D. SPIES, ALFRED A. WALKER and ARTHUR W. WOODS, J. A. M. A. **113**:1481 (Oct. 14) 1939.

In the families of 800 pellagrins seen in and about Birmingham, Ala., 194 children and infants showed evidence of the disease. The diets of the mother and of the whole household were inadequate, consisting chiefly of carbohydrates. Histories revealed that onset in infancy followed dietary deficiency in the mother during pregnancy and lactation.

In the cases presented as examples there were symptoms of diarrhea and loss of weight, as well as cutaneous lesions in infants and children with a history of dietary insufficiency. A therapeutic test made by administration of yeast, nicotinic acid or one of the pyrazine compounds gave prompt relief of the symptoms.

HEERSMA, Kalamazoo, Mich.

SUMMARY OF SOME CLINICAL STUDIES ON VITAMIN K. ERIK TAGE-HANSEN, J. A. M. A. **113**:1875 (Nov. 18) 1939.

The oral, intramuscular and intravenous administration of vitamin K is described for those conditions in which a prothrombin deficiency is present. This is of value in treatment of hypoprothrombinemia of the newborn and of older infants suffering from icterus gravis neonatorum and related diseases, such as hemorrhagic disease of the newborn.

HEERSMA, Kalamazoo, Mich.

HEMORRHAGIC SYNDROME APPARENTLY OF SCORBUTIC ORIGIN IN A BREAST-FED INFANT. H. JANET, ODIER-DOLLFUS, BARILLON-LAMOTTE and H. CAPELLE, Bull. Soc. pédiat. de Paris **37**:279 (May) 1939.

A boy aged 4 months had repeated hematuria and showed cutaneous petechiae. He was breast fed. The mother's diet was restricted. Bleeding ceased after a few days of an antiscorbutic regimen. Scurvy was believed to be the cause of the hemorrhage, although no evidence to support the diagnosis was obtained.

BENJAMIN, Montreal, Canada.

ACTION OF VITAMIN C ON ELIMINATION OF WATER IN NORMAL CHILDREN. R. CANNATA, Med. inf., Rome **11**:29 (Feb.) 1940.

From 0.20 to 0.50 Gm. of vitamin C was administered intravenously to normal children between 6 and 10 years of age. Prior to administration of the vitamin 500 cc. of water was taken by mouth. The volume of urine excreted was measured in thirty minute periods for two hours. By comparing the observations on the

subjects to whom vitamin C was given with observations on control subjects it was found that in 3 cases excretion of urine was the same with and without vitamin C, and in 4 cases considerably less urine was eliminated after the vitamin C had been given. Cannata explains the diminished diuresis on the basis of modifications of carbohydrate metabolism. The results are somewhat surprising, as scurvy is usually accompanied by edema, and one would expect that vitamin C would lead to more rapid elimination of fluid.

HIGGINS, Boston.

STUDIES ON THE URINARY EXCRETION OF ASCORBIC ACID IN NORMAL INFANTS. E. INGLESSI and A. AFENDAKI, Riv. di clin. pediat. **38**:217 (April) 1940.

As many as 365 determinations of the ascorbic acid content of the urine were made for 116 infants. The excretion of ascorbic acid in the urine tends to be less during the second trimester of life than during the first. It also is less in children showing some congenital debility. Therefore, the need for vitamin C is greater in children in the second trimester of life and in those who are congenitally debilitated.

HIGGINS, Boston.

RELATION OF RICKETS TO TETANY. E. HENNIG, Ztschr. f. Kinderh. **61**:379 (Oct. 5) 1939.

Examinations of 140 infants revealed that in only 17.8 per cent is the metabolic disturbance purely rachitic; in 82 per cent, tetany (in 31 per cent latent and in 69 per cent manifest) was also present. In only 40 per cent of the cases of tetany was the value for inorganic serum phosphorus more than 4 mg. per hundred cubic centimeters. A number of infants showed values corresponding to the lowest observed in cases of pure rickets. Increased (absolute or relative) phosphorus is thus not always associated with tetany and cannot be considered important in causing the appearance of tetanic manifestations. The observations contradict the theory that tetany is a healing stage of rickets.

SIEMSEN, Chicago.

Hygiene; Growth and Nutrition; Public Health

FACTORS IN THE GROWTH OF GIRLS. FRANCES A. MULLEN, Child Development **11**:27 (March) 1940.

The intercorrelations of seventeen physical measurements of girls of the ages of 7, 9, 11, 13, 15 and 17 years were analyzed by the Holzinger bifactor technic of factor analysis. At each age level a general factor and two group factors were found. The general factor accounts for from 30 to 50 per cent of the total variance of the seventeen measurements. Its loadings are fairly consistent throughout the various age groups. Estimates of it made from the factor pattern for one age show high correlation with estimates based on that for another. One group factor is found in the residual correlations between the height, the span of the arms, the length of the forearm and the length of the lower part of the leg. The other group factor was found in the residual correlations between weight, bi-iliac and bitrochanteric diameter and chest girth, width and depth. These factors have also been estimated, although the group factors as estimated by regression equations calculated from different factor patterns do not correlate as highly with each other and do not give as nearly similar mean growth curves as do the various estimates of the general factor. The growth of the factors, both general and group, was studied separately for groups of girls classified according to age at the menarche. Significant differences in the growth of the various factors were found between such groups.

MULLEN, Chicago.

INFANT MORTALITY IN THE FIRST TWO YEARS OF LIFE AND HOW TO DIMINISH IT: ANSWERS TO QUESTIONNAIRE. Lattante **10**:120 (March) 1939.

A summary of answers to a questionnaire sent to pediatricians in Italy regarding the reduction of infant mortality is given. The questionnaire presented the following outline:

1. Factors influencing infant mortality
   (*a*) Prenatal
   (*b*) Postnatal
2. Principal causes of infant mortality in the first two years of life
   (*a*) Constitutional illnesses (congenital and neonatal)
   (*b*) Illnesses of the digestive system
   (*c*) Illnesses of the respiratory system
   (*d*) Infections and other causes
3. Hygienic and social measures for decreasing infant mortality
4. Propaganda and public health activities in their reflection on infant mortality

Infant mortality in Italy is between 100 and 110 per thousand live births. This is a much higher rate than that in England, 60; the United States, 59; Sweden, 49; Switzerland, 48; Norway, 47; Australia, 42, or New Zealand, 32. Of the deaths occurring in 1936, 30 per cent were due to diseases of the digestive tract; 27 per cent to constitutional ailments, i. e., congenital disorders and disorders present in the newborn; 25 per cent to diseases of the respiratory tract, and 18 per cent to infections and other causes. The various causes and suggested remedies are discussed.

Some answers to the questionnaire are being published in subsequent numbers of this journal.

HIGGINS, Boston.

ORGANIZATION AND RESULTS OF CHILD WELFARE SERVICES IN URUGUAY. ROBERTO BERRO, Bol. Inst. internac. am. de protec. a la infancia **13**:349 (Oct.) 1939.

"Without failing to recognize that there is yet much to be done (and that even if we realize great work, we will never arrive at what ought to be done, for the possibilities of child and family welfare are almost infinite), there is no doubt that in our country, technically and practically, in the organization of child welfare services, within all medical, juridical, pedagogical and social fields a well aimed route has been followed, a net and straight one, the two principal characteristics of which are 'Unity of Action' (from gestation up to the majority of age) and 'Legal Basis,' both granted by the Children's Code, proclaimed as law of the nation on April 6, 1934."

AUTHOR'S SUMMARY.

BIRTH RATE AND THE RIGHTS OF THE CHILD, BUENOS AIRES. ERNESTO NELSON, Bol. Inst. internac. am. de protec. a la infancia **13**:529 (Jan.) 1940.

The author is inclined to believe that the normal birth rate of mankind is necessarily low. It was so from the far-off origins up to the sixteenth century and ought to be hereafter, unless it is desired that the opportunities for life in a few more centuries be restrained in a degree incompatible with human instincts.

What has happened is that the time of imperceptible growth in the multiplication of mankind experienced an unexpected increase when geographic discoveries, industrial development and commerce offered to the man of the western hemisphere new and unforeseen opportunities for life and action. The proletarian then discovered the possibility of increasing his economic comfort with the help of numerous offspring. The extraordinary increase in the European population, which from fifty million inhabitants in the fifteenth century rose to one hundred

and eighty million at the beginning of the nineteenth and to five hundred million in 1930, was due to the plebeian class. The middle and aristocratic classes are reproduced in a degree scarcely sufficient to keep the population stationary.

It is a well known fact that the suburbs of the cities and the poorest districts of countries show the highest birth rate. The author proves from recent statistics that this is true in Buenos Aires.

According to the author, the descent in the birth rate takes place when the human masses start to become educated and when a conscience is formed as to family responsibility and the rights of the child to health, education and welfare are recognized. The laws for school attendance, hygienic protection, prohibition of work at an early age, every day stricter, are not compatible with numerous offspring.

FROM EDITOR'S SUMMARY.

THE HOUSE OF ASSISTANCE "ALEJANDRO DEL RIO" AND THE SOCIAL MEDICAL ASSISTANCE TO CHILDREN IN RURAL AREAS. MANUEL ZORRILLA, Bol. Inst. internac. am. de protec. a la infancia **13**:774 (April) 1940.

The difficulties of the health problem in rural communities depend on (1) the low wages received, (2) the lack of culture and knowledge of hygiene and (3) the scattered nature of the population. The physician and his assistants can act only indirectly to correct the first condition. Their responsibility is direct in the matter of hygienic knowledge, and the third difficulty may be met by developing special travel units.

LESLIE, Evanston.

PREVENTIVE SOCIAL ASSISTANCE TO THE CHILD IN A STATE OF MORAL DANGER. JOSEFINA TOLOSA DE MONTELLANO, Bol. Inst. internac. am. de a la infancia **13**:848 (April) 1940.

As means for giving preventive social assistance the author cites the school and the behavior clinic, in which she believes that the psychiatric physician, the physiologist, the teacher and the social worker must intervene and collaborate, trying to find specially for the child the fundamental elements for living: food, clothes, hygienic dwellings, etc.

In Chile the "Council on Behalf of the Child" was established in May, 1934. It has performed since then a real preventive work by means of two services, the open assistance service and the closed assistance service.

The open assistance service protects the child without removing it from the home; this protection is afforded by the "centers of defense," which the children attend all day, receiving adequate nourishment and having large places for recreation. In these centers 6,804 children are assisted.

The aim of the closed assistance service is to help the orphan, the deserted child or the child who, for any reason, cannot live with his parents. For this purpose a "central house" and four establishments with a capacity for 1,400 children have been organized, as well as a service for the placement of children in homes, which have given very good results.

FROM EDITOR'S SUMMARY.

GENERAL SCALE OF "INFANTO-PUERILE" VALUES. JOSÉ MARÍA ESTAPÉ, Bol. Inst. internac. am. de protec. a la infancia **13**:884 (April) 1940.

The "bio-psycho-mesological and historical" method, applied to the study of the evolutive personality of the child and the adolescent, is the only prolific method that might lead to the absolute integral and synthetic knowledge of the "infanto-puerile age" (infancy and youth).

Regarding functional and constitutional pathology, only the integral knowledge is real and fecund; partial and fragmentary knowledge is always hopelessly false and sterile.

FROM EDITOR'S SUMMARY.

Prematurity and Congenital Deformities

HEREDITARY CLEIDOCRANIAL DYSOSTOSIS WITH FEATURES OF OCULAR HYPERTELORISM. ELI RUBENS, Arch. Pediat. **56**:771 (Dec.) 1939.

Two cases of cleidocranial dysostosis with features of hypertelorism are reported. They were seen in members of the same family, a girl aged 9 years and her father, aged 50 years. A family history of this disturbance can be traced for five generations.

ORR, Buffalo.

THE USE OF ESTROGENIC SUBSTANCE IN THE TREATMENT OF THE PREMATURE INFANT. MARCUS B. EINHORN, Arch. Pediat. **57**:115 (Feb.) 1940.

Fourteen premature infants were given an estrogenic substance to evaluate this method of preventing loss of weight after birth and aiding a more rapid return to birth weight. A control group of an equal number of babies was also observed.

The treated group showed an average loss of 4.3 ounces as compared with 6.9 ounces in the control group. The return to birth weight in the treated patients required twelve and seven-tenths days and in the control subjects seventeen days.

ORR, Buffalo.

CONGENITAL HEMI-HYPERTROPHY. J. HENSON, South African M. J. **13**:743 (Nov. 11) 1939.

The author briefly reports a case of congenital hemihypertrophy in a girl 14 years of age.

GONCE, Madison, Wis.

CLEIDOCRANIAL DYSOSTOSIS. R. DEBRÉ, M. LAMY and G. SÉE, Ann. de méd. **46**:5 (June) 1939.

Study of 5 cases of cleidocranial dysostosis disclosed that the clavicular and cranial malformations are accompanied as a rule by other malformations of the bony structure, among which pelvic malformations are the most frequent, with those of the face and spinal column following. In discussing the origin of cleidocranial dysostosis, Debré and his associates state that it is not connected with any infection, in particular not with syphilis, that it is not a bone disease of membranous origin, that it is not connected with a malformation or lesion of the uterus or the membranes of the ovum and that it is not the consequence of oligohydramnios. Cleidocranial dysostosis is a genotypic dystrophy, which seems to be transmitted as a dominant mendelian characteristic.

J. A. M. A.

A CASE OF DOLICHOSTENOMELIA (MARFAN'S DISEASE) IN A BACKWARD CHILD. M. WAHL and M. SCHACHTER, Arch. de méd. d. enf. **43**:37 (Jan.-Feb.) 1940.

Using the term dolichostenomelia, which designates a condition now occasionally mentioned in the literature as arachnodactylia, Marfan (1896) described a clinical picture, congenital and familial, characterized by elongation and thinning of the bones, most marked at the distal extremity. There are also abnormal increase in stature, hypotonia of the muscles and reduction of the panniculus adiposus. The patients are dolichocephalic, with a flat and narrow chest, and are apt to show kyphosis or kyphoscoliosis. About 150 cases of this disorder have been recorded. An instance of the occurrence of the disease in a girl of 15 years is reported.

AMESSE, Denver.

CONGENITAL GIANT GROWTH OF THE SECOND LEFT TOE. C. HEMPEL, München. med. Wchnschr. **85**:331 (March 4) 1938.

Hempel reports a case of congenital overgrowth of the second left toe. Roentgenograms showed that the second left metatarsal bone was wider and longer than

the corresponding one of the right foot. The phalanges of the involved toe were much longer and wider than the corresponding ones of the right foot. The toe was amputated.

BRAHDY, Mount Vernon, N. Y.

Newborn

SEPSIS OF THE NEWBORN INFANT. MAURICE L. BLATT and A. ALVIN WOLF, J. Pediat. **14**:695 (June) 1939.

Despite the sharp drop in the general morbidity and mortality rate in infancy and childhood during the last fifty years, the rate during the first month of life has remained almost stationary. One of the causes of this high neonatal rate is sepsis. The incidence of deaths from sepsis has not been reduced. On the contrary, epidemics, apparently of sepsis, have occurred with increasing frequency among the neonatal group in hospitals previously free from infections. The authors believe that the epidemics which have been classified as epidemics of diarrhea among newborn infants and which have been reported from all parts of the United States are truly epidemics of sepsis. The fact that newborn infants have a low resistance to pyogenic organisms and that infection with this group of organisms is often accompanied by frequent stools makes an assumption of "sepsis" as a primary disease seem more logical than a diagnosis of primary diarrhea. An epidemic of this type is reported, in which 2 of 3 nurseries for newborn infants were involved. Twenty-seven infants showed septic symptoms when 277 other newborn infants were unaffected. Of those infected, 7 died. Postmortem examination of the 7 who died showed bronchopneumonia in 6, and in only 2 was there anatomic evidence of enterocolitis. Multiple abscesses were observed in 2 and endocarditis in 1. Bacteriologic studies of the cardiac blood and of the gastrointestinal tract made post mortem showed a variety of organisms. Similar studies of the blood and stools of those who survived also yielded a variety of organisms, and no correlation was found when comparison was made with the results of autopsy studies. Consequently the causation of this epidemic, as of all those previously reported, cannot be ascribed to a single organism.

RAUH, Cincinnati.

THE VALUE OF ROENTGENOGRAPHIC EXAMINATION IN THE DIAGNOSIS OF SYPHILIS IN NEWBORN INFANTS. AMOS U. CHRISTIE, J. Pediat. **15**:230 (Aug.) 1939.

Eighty-three infants born of syphilitic mothers were studied by roentgen examination of the long bones in an effort to determine the value of this method of examination for early and accurate diagnosis of congenital syphilis. A diagnosis of syphilis later shown by clinical and serologic follow-up to be correct was made early in only 2 cases. In 47 cases a diagnosis of "no syphilis" was made, which was later shown to be correct. In 23 cases the diagnosis was recorded as "doubtful." Christie discusses the changes found in the bones on roentgen examination which gave rise to the roentgenographic diagnosis of "doubtful." Deposition of bismuth in the bones of the fetus as a result of treatment of the mother with a bismuth compound, severe illness of the mother or rapid growth of the infant after birth may cause osseous changes which will simulate changes thought to be due to syphilitic infection. Therefore it is advisable to confirm the roentgen findings by clinical and serologic examinations before a definite diagnosis of syphilis is made and treatment for the disease begun.

RAUH, Cincinnati.

TETANUS NEONATORUM: REPORT OF A CASE WITH RECOVERY. D. B. MONSKY, South. M. J. **33**:67 (Jan.) 1940.

The author states that tetanus neonatorum was once the greatest single cause of neonatal mortality. The portal of entry is almost always the umbilical cord.

"The treatment," he writes, "consists of: (1) neutralization of the toxin by using large doses of tetanus antitoxin; and, (2) control of the clonic spasms which lead to exhaustion and death. . . . On account of the difficulty in opening the mouth, feeding by dropper or gavage must be resorted to."

The mortality rate of tetanus neonatorum is extremely high. Recovery is unusual.

F. W. SCHLUTZ, Chicago.

ANEMIA OF THE NEWBORN. H. L. DWYER and F. C. NEFF, South. M. J. **33**:246 (March) 1940.

Dwyer and Neff state, in their summary:

"Two newborn infants with anemia associated with erythroblastosis and icterus are described, in which blood transfusion was followed promptly by a return to normal. One newborn with anemia, in whom erythroblastosis and icterus were not present, did not respond to repeated transfusions. The use of liver extract hypodermatically was followed by the appearance of reticulocytes and immature granulocytes immediately, with a gradual return to normal blood values. This suggests that erythroblastic-hemolytic anemia of the newborn is differentiated from the non-erythroblastic type not only clinically, hematologically and pathologically, but, possibly, also by the response to intravenous blood."

F. W. SCHLUTZ, Chicago.

Acute Contagious Diseases

DIPHTHERIA PATCH TEST POSSIBILITIES. ROBERT COHEN and JAMES W. BRUCE, Arch. Pediat. **57**:53 (Jan.) 1940.

A dose of Schick test toxin incorporated into an oil base fails to produce any cutaneous reaction when used in a patch test of children known to react positively to the Schick test. However, there is an iota of hope in incorporating this dose with a rubefacient and vesicant substance.

ORR, Buffalo.

MUMPS MENINGO-ENCEPHALITIS. AN ANALYSIS OF TWENTY-NINE CASES. SIDNEY H. TABOR and BENJAMIN NEWMAN, Arch. Pediat. **57**:133 (March) 1940.

Twenty-nine cases of meningoencephalitis complicating mumps are reviewed. Five of the patients were girls and 24 were boys. The majority were in the 5 to 10 year group.

The chief signs and symptoms were frontal headache, nausea, vomiting and rigidity of the neck.

Meningoencephalitis may occur before, during or after the onset of swelling of the parotid glands.

Rapid recovery was noted in all cases. However, on follow-up 9 patients showed evidence of minor mental changes.

ORR, Buffalo.

DETOXIFIED ANTIGEN IN THE TREATMENT OF PERTUSSIS. MANFRED WEICHSEL and JOSEPH H. LAPIN, Arch. Pediat. **57**:159 (March) 1940.

One hundred and seventy-six children with active whooping cough were treated by the administration of "detoxified pertussis antigen." Injections were given every two to three days in doses ranging from 0.3 to 2 cc. The average total dose was 4 to 5 cc. A beneficial response was observed in 56.3 per cent of the patients treated. The average duration of the disease seemed to be definitely shortened. The average number of paroxysms among the children treated with pertussis antigen was less than that among the control subjects after three weeks of the disease.

Fifty-seven children were inoculated with three to six doses of "detoxified pertussis antigen" after intimate contact with persons having whooping cough. Most of these patients were in homes where there was frequent and intimate contact with one or more members of the family suffering from the disease. Thirty-seven children remained free from symptoms, 11 had a mild form of the disease and 9 had pertussis of average severity.

Realizing that the statistical evidence submitted was meager and that no passive conclusions may be drawn, the authors feel that the results were favorable enough to warrant the use of "detoxified pertussis antigen" in the treatment of active whooping cough and in the protection of susceptible children who have been recently exposed.

ORR, Buffalo.

SMALLPOX VACCINATION OF INFANTS. HARRY H. DONNALLY, J. A. M. A. **113:** 1796 (Nov. 11) 1939.

Successful vaccinations were carried out on 70 newborn infants, and they were revaccinated two to three years later. Half were inoculated at birth with calf lymph virus and half with culture virus (Rivers). Successful protection was determined by the development of an accelerated reaction or a less severe reaction at the time of revaccination with calf lymph virus. Only 2 of the 36 children inoculated with culture virus showed substantial immunity after two to three years, while 25 of 34 successfully inoculated at birth with calf lymph virus showed substantial immunity.

Although the critical test of exposure to smallpox is the absolute requirement for comparison, calf lymph virus can give adequate protection to newborn babies.

HEERSMA, Kalamazoo, Mich.

PROPHYLAXIS AGAINST WHOOPING COUGH IN EXPOSED CHILDREN, WITH SPECIAL REFERENCE TO SERUM. PHILIP COHEN and JOSEPH LAPIN, J. Pediat. **15:**78 (July) 1939.

The authors conclude their report as follows:

"1. Over 100 children directly exposed to whooping cough were treated with various prophylactic measures.

"2. Intensive daily therapy with Sauer's vaccine had no noticeable effect on the incidence or course of whooping cough in exposed cases.

"3. Krueger's vaccine was similarly ineffective.

"4. Topagen (Mulford, soluble) had no apparent effect, given in 3 c.c. doses.

"5. Adult blood serum was effective in 61 per cent of our subjects intimately exposed to whooping cough. The course of those who contracted the disease after injection was generally modified. The doses recommended are 20 c.c. for infants and 40 c.c. for older children.

"6. Hyperimmune serum can be obtained from an individual with a history of having had whooping cough after he has been inoculated with large doses of vaccine (20 c.c.) over a period of six to eight weeks. Serum is obtained one or two weeks later. Such serum protected two-thirds of our cases, and modified the rest, though intimately exposed to the disease.

"7. Convalescent serum was found to be the most effective prophylactic agent in children exposed to whooping cough. We advise 15 c.c. to 20 c.c. for an infant and 40 c.c. for an older child."

RAUH, Cincinnati.

A STUDY OF THE VIRUS FACTOR IN WHOOPING COUGH. J. M. FRAWLEY, J. Pediat. **16:**18 (Jan.) 1940.

In spite of the accumulation of evidence establishing the Bordet-Gengou organism as the sole etiologic agent in whooping cough, the question of the role of a filtrable virus in producing the clinical and pathologic picture of this disease has not been

finally settled. Frawley carried on a series of experiments in which 12 children were given nasal instillations of filtered washings taken directly from the respiratory passages of children suffering from whooping cough. Cultures made from the nasal washings prior to and after filtration were positive for Haemophilus pertussis before filtration and negative for this organism after filtration. In 8 cases no noticeable result followed the instillation of the filtered washings. In 4 cases there was a slight rise of temperature. In 2 cases coryza and a cough developed. In no case did any symptoms resembling whooping cough develop.

RAUH, Cincinnati.

SUMMARY OF THE CURRENT PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **55**:107 (Jan. 19) 1940.

For the period of Dec. 3 to 30, 1939, there was an increase in influenza to three times the incidence in the same period in 1938. The incidence of poliomyelitis was also three times that of the corresponding period in 1938, but had declined 50 per cent. Other contagious diseases were below the median prevalence. The mortality from all causes was 11.2 per thousand, which is below the average.

SANFORD, Chicago.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **55**:799 (May 10) 1940.

For the period from March 24 to April 20, 1940, the incidence of all eight of the communicable diseases was below the seasonal expectancy. The average mortality rate was 12.2 per 1,000 as compared to 12.4 for the five preceding years.

SANFORD, Chicago.

DIPHTHERIA IN TENNESSEE. W. V. SANFORD, RUTH R. PUFFER, C. B. TUCKER and A. E. HARDISON, South. M. J. **33**:321 (March) 1940.

In the concluding paragraphs the authors state:

"The field epidemiologic records of 1,446 cases reported as diphtheria from forty counties of the State of Tennessee were studied. . . .

"In the majority of cases, physicians were not called early enough for treatment to do the maximum of good. The health departments should stress the importance of calling physicians early in throat affections, particularly in cases having laryngeal symptoms.

"Continued stress should be laid on the protection of children early in the preschool period, especially in poor, isolated homes. . . .

"It is possible that one dose of alum toxoid is not sufficient to prevent cases and deaths in a sufficiently high percentage of children to maintain confidence in the procedure on the part of health departments. . . .

"In none of the counties was diphtheria eliminated as a problem. Though the disease was prevalent almost continuously, no major outbreaks occurred in any of the counties."

F. W. SCHLUTZ, Chicago.

ACUTE ANTERIOR POLIOMYELITIS IN SOUTH CAROLINA IN 1939. W. WESTON JR., South. M. J. **33**:525 (May) 1940.

The author described an epidemic of poliomyelitis in South Carolina. Lumbar puncture is advised as a method of diagnosis and treatment. No specific therapy is offered. Vitamin B_1 offers no specific benefit when used in large quantities. Plenty of orange juice, tomato juice or lemonade should be drunk to insure an abundant intake of vitamin C. The use of ultraviolet rays is beneficial because of its triple action (it is virucidal; it activates cholesterol, and it produces cornification of the nasal mucous membrane).

Drugs, including sulfanilamide and its derivatives, do not provide specific cures. Operations, such as tonsillectomies and operations for hernia, are advised against during an epidemic unless there is an emergency.

Negroes proved just as susceptible as white persons in the South Carolina epidemic.

SCHLUTZ, Chicago.

THE MODERN TREATMENT OF BACILLARY DYSENTERY. H. F. GARRISON JR., South. M. J. **33**:533 (May) 1940.

The author reports that, although the prevalence of bacillary dysentery has been decreased, many sections of the South continue to have a relatively high incidence of the disease. The incidence of bacillary dysentery is proportionate to the sanitary conditions of the community and to personal hygienic conditions.

Diets low in fat content are universally considered best. Reported results with high protein, high carbohydrate or intermediate diets do not show any great differences. Early administration of sodium thiocyanate intravenously may have value, and further study of this method is advocated.

The prevention and treatment of the associated dehydration, acidosis and demineralization continue to be the most important factors for consideration.

SCHLUTZ, Chicago.

MEASLES COMPLICATING PREGNANCY. ISADORE DYER, South. M. J. **33**:601 (June) 1940.

The author reports that 24 cases of measles complicating pregnancy were observed over a period of three months. The age incidence ranged between 14 and 42 years.

Pregnancy was interrupted in 37.5 per cent of cases, in 25 per cent of which the patients were at or near term. Three babies exhibited measles at birth or two days afterward.

A laparotrachelotomy was performed on 1 mother at the height of her exanthem because of a pelvic contraction and persistent labor.

There was no maternal mortality, but there was 1 instance of morbidity due to sequelae.

SCHLUTZ, Chicago.

A NEW TREATMENT OF POLIOMYELITIS. J. TREMBLAY, Union méd. du Canada **69**:35 (Jan.) 1940.

The remarkable success which Contat has obtained in Switzerland in the treatment of poliomyelitis with potassium chlorate led Tremblay to investigate the usefulness of this drug. When it is given to a patient with typical signs of acute poliomyelitis the temperature falls, the stiffness of the neck disappears, headache vanishes and beginning paralysis is halted.

In experiments on monkeys which were inoculated intracerebrally, complete protection against paralysis was obtained in all but 1 case. In this case the monkey refused to take the potassium chlorate after four and three-fourths days. Forty-eight hours later quadriplegia developed. Three control animals were studied at the same time; of these, 2 died and 1 was badly paralyzed.

The dose established is 8 to 10 cg. for each kilogram of body weight. This daily dose is divided into twelve portions given at two hour intervals. After the temperature drops, the dose is diminished one third and continued for forty-eight hours.

Tremblay cites pharmacologic opinions as to the low toxicity of potassium chlorate, in spite of the generally accepted bad reputation of the drug. He believes that the efficacy of potassium chlorate is due to its oxidizing activity.

DAFFINEE, Boston.

POLIOMYELITIS: III. THE USE OF MACACUS CYNOMOLGUS AS AN EXPERIMENTAL ANIMAL. F. M. BURNET, A. V. JACKSON and E. G. ROBERTSON, Australian J. Exper. Biol. & M. Sc. **17**:375 (Dec.) 1939.

The authors found cynomolgus monkeys to be highly susceptible to infection with poliomyelitis virus, infection by any route being invariably fatal and the cord taken from a prostrate cynomolgus monkey containing a higher concentration of virus than similar material from a prostrate rhesus monkey. Serum neutralization tests could be carried out as in rhesus monkeys by either intracerebral or intraocular inoculation, the latter method giving the more satisfactory results. Probably the most important of the observations in this study was that a large proportion of cynomolgus monkeys can be infected by simple swabbing of virus on the pharyngeal region. The histologic findings in cynomolgus monkeys inoculated by various routes are described. The lesions resemble those observed in rhesus monkeys but are more widely distributed and often show a more acute polymorphonuclear response.

GONCE, Madison, Wis.

SOME FACTORS INFLUENCING THE SPREAD OF SCARLET FEVER IN AN INSTITUTION. E. V. KEOGH, IAN MACDONALD, JOAN BATTLE, R. T. SIMONS and STANLEY WILLIAMS, J. Hyg. **39**:664 (Nov.) 1939.

In an outbreak of scarlet fever due to Streptococcus pyogenes type II, in Melbourne (Victoria, Australia), 59 children in a single ward were studied. Material from the throat was taken by swab weekly for ten weeks and again after an interval of thirteen weeks. In 16 patients scarlet fever with a rash developed, and in 23 the disease appeared without a rash (infection with Str. pyogenes type II).

The authors state in their summary: "Haemolytic streptococci were isolated at least once from all but four children.

"Seven group A strains and one group C strain were present in the ward. Two group A strains and the group C strain spread freely, but were not associated with scarlet fever or any evident clinical symptoms. . . .

"Children with and without tonsils were equally susceptible to infection with haemolytic streptococci, irrespective of group or type, but the infections persisted much longer in the children with tonsils.

"Sulphanilamide therapy did not check the epidemic."

JANNEY, Wauwatosa, Wis.

SUSCEPTIBILITY TO DIPHTHERIA AND POLIOMYELITIS. W. G. HEASLIP, M. J. Australia **2**:899 (Dec. 16) 1939.

The author reports an incidence of positive reactions to the Schick test of 83 per cent among children under 6 years of age with poliomyelitis and of 78.7 per cent among normal controls. In contrast, a group of children from 6 to 12 years of age with poliomyelitis showed an incidence of 70.6 per cent positive reactions to the Schick test, while controls in the same age group showed an incidence of only 40.2 per cent. Since the susceptibility to these diseases decreases with advance in age, the author concludes that these findings are evidence of a relation between susceptibility to poliomyelitis and susceptibility to diphtheria.

GONCE, Madison, Wis.

A BRIEF SURVEY OF SOME OF THE POLIOMYELITIS PATIENTS EXAMINED DURING THE VICTORIAN EPIDEMIC OF 1937-1938. S. WILLIAMS, M. J. Australia **1**:147 (Feb. 3) 1940.

Williams personally observed 133 patients with poliomyelitis. Of 66 patients seen in the preparalytic stage, only 15 (27 per cent) did not become paralyzed.

This small proportion of abortive conditions with which paralysis did not develop may indicate that the virus infections during the epidemic are confined more to cases of actual poliomyelitis than is generally considered to be the case.

GONCE, Madison, Wis.

ANTIDIPHTHERITIC IMMUNIZATION AT THE HOPITAL DES ENFANTS-MALADES FROM 1924 TO 1928. P. LEREBOULLET, P. JOANNON, G. BOULANGER-PILET, J.-J. GOURNAY and P. GRIPPON DE LA MOTTE, Bull. Soc. pédiat. de Paris **37**:248 (May) 1939.

Of the children who received two injections of toxoid, 88 per cent gave negative reactions to Shick tests six weeks after inoculation, while 98 per cent of those who were given three injections reacted negatively after a similar period. It is stated that no serious accident occurred after about 50,000 injections, although five abscesses at the sites of injections were observed. Local reactions were noted in 10 to 20 per cent of the patients and these never inconvenienced the children for more than a day or two. These reactions were not encountered in children under 5 years old. Sixty children who were given Schick tests six years after inoculation had negative reactions. Few cases of proved diphtheria in immunized children were recorded. A group who were given antitoxic serum and anatoxin almost simultaneously showed only 65 per cent to 70 per cent of negative reactions to Shick tests.

BENJAMIN, Montreal, Canada.

PATHOGENESIS AND TREATMENT OF MALIGNANT DIPHTHERIA. P. GIRAUD and HO-TA-KHANH, Presse méd. **47**:364 (March 8) 1939.

The authors classify the malignant phases of diphtheria under three types, according to the time of onset.

1. In the early forms the authors advise the use of antitoxin, strychnine, extract of adrenal cortex and (for the less severe conditions) ouabain. Toxoid is contraindicated.

2. Secondary complications occur after the membrane has sloughed, when palatal paralysis, vomiting or bradycardia ensues. To prevent these complications, the authors advise the use of toxoid in doses of 0.5 to 1.0 cc. every three or four days, beginning a couple of days after antitoxin has been given.

3. Later complications, coming on after forty or fifty days, are probably anaphylactic. The use of toxoid following antitoxin seems to prevent these complications.

DAFFINEE, Boston.

BISMUTH-LECITHIN THERAPY IN DIPHTHERITIC ANGINAS AND IN SUSPECTED DIPHTHERITIC ANGINAS. G. BETTINARDI, Med. ital. **20**:113 (March 31) 1939.

The complex bismuth-lecithin has a bactericidal effect on streptococci in the oral cavity. The preparation is well tolerated when given intramuscularly, as was shown by the author's use of it in 150 varied cases. The lecithin facilitates absorption of the bismuth and reduces its toxicity. The author reports on the use of bismuth-lecithin in a series. One hundred and fourteen patients were given bismuth-lecithin plus antidiphtheritic serum. The controls were given serum alone.

The diphtheritic forms of angina are not benefited by bismuth-lecithin. The nondiphtheritic forms of acute angina show rapid improvement in general symptoms, a fall in temperature and disappearance of exudate when the patient is given bismuth-lecithin.

The author believes that bismuth-lecithin plus serum should be given in all cases of angina with an exudate while a bacteriologic report on the culture of material from the throat is awaited.

MARTOCCIO, Utica, N. Y.

ANTITOXIC ACTION OF ASCORBIC ACID AND OF EXTRACT OF ADRENAL CORTEX AGAINST DIPHTHERIA. A. GALEOTTI FLORI, Riv. di clin. pediat. **37**:577 (July) 1939.

Experimental observations were made on guinea pigs. Ascorbic acid, alone or combined with an extract of adrenal cortex, has some detoxifying action in vitro against diphtheria toxin; this increases with the duration of contact. In vivo, also, there is some detoxifying action of ascrobic acid and cortigen, both separately and in combination. This is more marked if the animal is given the toxin some time after the other injections. Ascorbic acid seems to augment the action of diphtheria antitoxin.

HIGGINS, Boston.

CLINICAL AND THERAPEUTIC OBSERVATIONS ON POLIOMYELITIS. P. POLETTI, Riv. di clin. pediat. **37**:928 (Nov.) 1939.

In 1939 an epidemic of poliomyelitis prevailed in the Italian province of Mantova; 51 patients, 20 of them with severe disease, were treated in the isolation hospital. The case records of these patients are reviewed. None died; 20 recovered; 31 still showed residual paralysis at the time of writing. Forty-seven of the children were under 5 years of age.

The medical therapy consisted of intravenous or intramuscular injections of (1) convalescent serum, (2) adult serum or (3) serum and 30 to 60 cc. of cerebrospinal fluid from patients forty to sixty days convalescent. The results from the serum therapy are:

	Patients Cured	Patients Benefited	Patients Showing No Benefit
Convalescent serum.....	3	0	0
Adult serum.....	4	2	2
Serum and spinal fluid....	2	7	1

All of the patients received Marconi therapy (wavelength, 6 meters; distance of electrodes, 40 cm.); twenty treatments of ten to thirty minutes each were directed to the spinal column in the region believed involved.

HIGGINS, Boston.

PATHOGENESIS AND TREATMENT OF MEASLES. REYNALDO AGRELO, Rev. méd. latino-am. **25**:318 (Dec.) 1939.

A review is given of the present knowledge of the prophylaxis and treatment of measles with maternal blood, the serum of convalescents and placental extract.

DWYER, Kansas City, Mo.

STROPHANTHIN TREATMENT OF THE DIPHTHERITIC HEART. F. HANSEN, Kinderärztl. Praxis **10**:518 (Dec.) 1939.

All forms of diphtheritic lesions of the heart are treated with intravenous injection of strophanthin. The initial dose is from 0.1 to 0.15 mg. Strophanthin is given from one to three times a day. The immediate effect is observed. Injections are usually given three days in succession and omitted the fourth day. The action of the heart should be ausculted up to five minutes after the injection. A few extra systoles have no importance. Irregularities of longer duration, however, warrant diminution of the dose. Small doses are recommended because the heart of a patient with diphtheria is especially sensitive to strophanthin. The author believes that strophanthin is definitely superior to digitalis for such a patient.

HEYMANN, Cleveland.

ECZEMA VACCINATUM. H. ASPERGER, Wien. klin. Wchnschr. **36**:826 (Sept. 8) 1939.

A 9 month old girl had suffered for four months with seborrheic eczema. She was hospitalized on account of an outbreak of vesicles and a high fever. The clinical picture of eczema vaccinatum was confirmed by laboratory tests of the contents of the vesicles. Further investigation revealed that a 12 year old brother had been vaccinated two weeks before the exacerbation of the sister's eczema. Five days previously the boy himself had had a high fever and a large, running vaccination pustule, and during these days he had played with the infant.

The infection spread over the child's entire body, and she died on the twelfth day. The mother also had a few pustules and fever, in view of which the author believes a familial susceptibility to vaccine virus may have existed. Nevertheless, he recommends vaccination in early life as one way to prevent occurrences of this kind.

ABT, Chicago.

ROENTGENOTHERAPY OF PARALYSIS AFTER ACUTE POLIOMYELITIS. K. GEFFERTH, Orvosi hetil. **83**:636 (July 1) 1939.

The treatment should begin after the fever has ceased. The first doses should be small (10 per cent of the unit skin dose), and in order that the rays may reach the spinal cord, zinc or copper filters should be used. This dose can be given for two weeks, once weekly. When children in a later stage of paralysis come for treatment the doses can be raised (20 to 25 per cent of the unit skin dose). It is advisable to repeat the whole series of treatments after an interval of three weeks. So far this roentgen treatment has been tried in 27 cases. The author expresses the belief that in spite of the fact that it is difficult to estimate the effect of roentgenotherapy, dealing with this question is worth while.

GÖTTCHE, Budapest, Hungary.

Acute Infectious Diseases

A MALARIA SURVEY OF THE REPUBLIC OF COSTA RICA, CENTRAL AMERICA. HENRY W. KUMM and HORACE RUIZ S., Am. J. Trop. Med. **19**:425 (Sept.) 1939.

The authors examined 9,126 children in one hundred and sixty-eight different localities, using the technic described by Boyd and Aris for palpating the spleen. In a number of villages they obtained splenic indexes of more than 40 per cent, but Guanacaste was found to be the most malarial province in Costa Rica (Central America).

Blood films were obtained from every child who had a palpable spleen. Mixed infections were associated with the highest degree of splenomegaly. As the size of the spleen increased so did the percentage of positive results of examination of blood films. The places with a high degree of endemic malaria were generally at elevations of less than 1,000 feet.

Plasmodium vivax and Plasmodium falciparum were found throughout the malarial regions, but Plasmodium malariae was more common in the Pacific littoral region. Fifteen species of anopheles were obtained in 175 localities studied. Anopheles albimanus was abundant in all the regions where endemic malaria occurred and was the species most commonly taken inside houses and traps. It was also the only anopheline mosquito to be found naturally infected with malarial parasites.

BURPEE, Augusta, Ga.

CLINICAL TRICHOCEPHALUS TRICHIURUS INFECTION. J. CLYDE SWARTZWELDER, Am. J. Trop. Med. **19**:473 (Sept.) 1939.

The author analyzed the cases of 81 patients with uncomplicated clinical infection due to Trichocephalus, admitted to the Charity Hospital in New Orleans

over a fifteen year period. More than two thirds of the infections occurred in children between the ages of 6 and 15. White patients predominated over Negroes in the ratio of 5 to 1 and females over males in the ratio of 2 to 1.

The most frequent symptoms were abdominal or epigastric pains, vomiting, constipation, distention, flatulence, fever, headache, backache, loss of weight and anorexia. The duration of symptoms was three months or less in over 50 per cent of the cases. The most frequent clinical diagnosis was intestinal parasites, with chronic appendicitis second. Examination frequently revealed abdominal tenderness without rigidity, increase in the number of polymorphonuclears and an average eosinophil count of 4.2 per cent. In only 7 cases was the temperature above 101 F.

BURPEE, Augusta, Ga.

MALARIA RECONNAISSANCE OF THE PROVINCE OF ORIENTE IN CUBA. HENRY P. CARR, JOAQUÍN FERNÁNDEZ MELÉNDEZ and ALBERTO ROS, Am. J. Trop. Med. **20**:81 (Jan.) 1940.

The authors surveyed the province of Oriente and part of the provinces of Pinar del Río and Habana.

In the province of Oriente they examined 22,203 children for splenomegaly and 9,713 blood films for malarial parasites. Eight per cent of the children had enlarged spleens, and 1 per cent of the blood films showed malarial parasites. These parasites were several times more frequent in children with palpable spleens and many times more frequent in those with enlarged spleens than in those with normal spleens.

Five species of anopheles were encountered: Anopheles albimanus, Anopheles crucians, Anopheles grabhami, Anopheles vestitipennis and Anopheles atropos. Since A. albimanus was always present in large numbers where malaria was encountered, it was considered the most important vector in Oriente.

BURPEE, Augusta, Ga.

PARASITOLOGY; A ROUND TABLE DISCUSSION. ERNEST CARROLL FAUST, Ann. Int. Med. **13**:1230 (Jan.) 1940.

The topics discussed are: (1) amebiasis and infections due to intestinal flagellates, (2) intestinal helminthiases and (3) pulmonary disease, with respect to the role of animal parasites.

The symptoms, diagnosis and treatment of the most common representatives of each group are considered. Questions and answers accompany the article.

READING, Galveston, Tex.

MORE TULAREMIA REPORTED. Health News **17**:9 (Jan. 15) 1940.

Three cases are reported, in all of which the patients were adults: 1 was observed in Suffolk County (N. Y.), of tularemia due to an infection from a wild rabbit; 1 in Broome County (N. Y.), of tularemia transmitted through a bite of a deerfly, and the third in St. Lawrence County (N. Y.), in which the disease was due to an infection from a wild fox. In view of such wide distribution it is urged that physicians send samples of blood from all patients with suggestive symptoms to an approved laboratory for examination for Bacillus tularensis.

AIKMAN, Rochester, N. Y.

ACUTE INFECTIOUS JAUNDICE. JOHN A. NORTON, J. A. M. A. **113**:916 (Sept. 2) 1939.

In an epidemic of 23 cases of jaundice in one city (10 patients were children; average age, 14 years), the disease in most instances could be traced to contact with the patient in the initial case. The differentiation of the condition in these cases from Weil's disease was made by means of agglutination tests and from catarrhal jaundice by the fact that an epidemic occurred.

Clinically the conditions in most cases were alike, with an onset of nausea and vomiting followed by abdominal pains and diarrhea in twenty-four hours. The temperature was about 100 F., and the patient became jaundiced in about a week, with the urine turning dark and the stools clay colored. There were few complications, but convalescence lasted about four weeks.

HEERSMA, Kalamazoo, Mich.

BACILLARY DYSENTERY. H. M. GINSBURG, E. M. HIRSCHBERG and FLORENCE BRISKER, J. A. M. A. **113**:1321 (Sept. 30) 1939.

In an epidemic of bacillary dysentery chiefly of the Flexner type occurring in 39 children 3 months to 8 years of age a characteristic blood picture was observed. Except in the late stages of the disease the Schilling index showed a 95 to 100 per cent shift to the left, although the total white blood cell count varied. The shift returned to the right as the disease progressed.

HEERSMA, Kalamazoo, Mich.

ISOLATION OF BRUCELLA FROM LYMPH NODES. M. A. POSTON and P. B. PARSONS, J. Infect. Dis. **66**:86 (Jan.-Feb.) 1940.

A method used successfully for the isolation of Brucella from lymph nodes is described in detail.

Lymph nodes from 10 of 19 patients with Hodgkin's disease yielded positive cultures of Brucella. Seven of the positive cultures were of the suis variety and 3 were of the melitensis.

"Cultures of lymph nodes from 3 patients with chronic brucellosis without clinical evidence of Hodgkin's disease were positive for Brucella melitensis var. melitensis in 2 instances and Brucella melitensis var. suis in 1.

"In a control series of cultures from 67 lymph nodes which were biopsied for a variety of causes Brucella melitensis var. suis was isolated from only 1."

AUTHORS' SUMMARY.

TREATMENT OF TYPHOID FEVER WITH VITAMIN A. PAUL GIRAUD and ANDRÉ VALLETTE, Arch. de méd. d. enf. **42**:691 (Nov.-Dec.) 1939.

In the absence of specific treatment, the management of typhoid fever has advanced but little. At Marseilles (France), where the water supply is frequently polluted, the type of fever is severe and the mortality approaches 20 per cent. Recently Chevallier called attention to the striking resemblance (in certain features) of typhoid fever and vitamin A deficiency. Among these manifestations he cites the peculiar dryness of the skin and the frequency of cutaneous abscesses. Investigation of ocular signs was not feasible in cases of serious attacks. It is recognized that the dietetic regimen universally followed includes large amounts of vitamin C in the various fruit juices but scant vitamin A in cases in which milk is not well tolerated. There are also identical alterations in the chronaxia, and examination of the blood during life and of the liver post mortem shows diminution of vitamin A, which amounts to complete disappearance in certain cases. With these observations in mind one could speculate on the possible changes following the enrichment of the organism with this vitamin. A series of 71 hospitalized patients were studied in 1936 and 1937. Vitamin A was administered both in the form of cod liver oil containing at least 2,000 units per cubic centimeter in doses of 10 to 20 drops daily and through intramuscular injection with a 3 per cent solution. Eschars and other cutaneous lesions were treated with local applications of cod liver oil.

Of the 71 patients, with all types of typhoid fever, 46 recovered without complications or relapse. There was no striking moderation in the course of the disease. Eighteen patients suffered from complications but went on to complete recovery. Eight patients died, a mortality of 11 per cent. There were no instances

of intestinal hemorrhage after vitamin therapy was begun, and only 1 patient suffered from perforation. The authors feel that the reduction in mortality, from 20 per cent to 11 per cent, is distinctly encouraging. AMESSE, Denver.

EARLY INFANTILE, POSTINFECTIOUS KOKARDEN PURPURA. H. SEIDLMAYER, Ztschr. f. Kinderh. **61**:217, 1939.

Ten cases, in 9 of which the disease followed prolonged grippal infections and in 1, primary tuberculosis, are reported. Several good photographs of the cutaneous lesions are published. The primary lesions were urticarial. On these there developed hemorrhages which resembled fleabites and which spread laterally. Centrally, a small nodule remained. At the periphery was an anemic zone. Frequently several crops of lesions were observed. In some cases there was edema surrounding the dermal lesions or over the dorsa of the hands and feet. Hemorrhages from the mucous membranes and colic were not observed. In 1 case transient hematuria was present. The platelet count was normal in 4 cases; in 3 cases the platelets numbered from 200,000 to 300,000, and in 3 there was definite thrombopenia, the count in 1 case being below the critical level of 30,000. In this case, however, a return to normal occurred in eighteen hours. The purpura is apparently allergic. In all cases except 1, in which death was due to miliary tuberculosis, the patient recovered and no recurrences were observed.

SIEMSEN, Chicago.

Diseases of Blood, Heart and Blood Vessels and Spleen

SIMPLE TACHYCARDIA IN CHILDREN. R. A. LYON and LOUISE W. RAUH, J. A. M. A. **113**:1121 (Sept. 16) 1939.

Ten children observed for periods up to seven years were repeatedly found to have pulse rates exceeding 115 per minute. All were preadolescent. In the 9 girls, thyroid disturbance (in 2), the onset of menstruation (in 6) and malnutrition (in 2) were in evidence, and in the 1 boy glandular obesity occurred. All these children had normal cardiac findings, and growth and development were unimpaired. The tachycardia subsided in most cases. HEERSMA, Kalamazoo, Mich.

PROTHROMBIN TIME DETERMINATION. ORVILLE R. KELLEY and W. E. BRAY, J. Lab. & Clin. Med. **25**:527 (Feb.) 1940.

Either capillary or venous blood may be used in determining prothrombin time. If the former is employed 0.5 cc. is needed. It can readily be obtained from the heel. The technic of the test is given in detail. READING, Galveston, Tex.

A COMPARATIVE STUDY OF THE ERYTHROCYTE SEDIMENTATION TEST WITH THE HELLIGE-VOLLMER (LANGER) MICROSEDIMETER AND THE MODIFIED WESTERGREN METHOD. ESTHER W. GOLDBERGER, J. Lab. & Clin. Med. **25**:657 (March) 1940.

The microsedimeter is useful in determining the sedimentation rate in children. The method requires only two or three drops of blood. It compares favorably with other methods. The apparatus and technic of the test are described.

READING, Galveston, Tex.

LEDERER'S ANEMIA. F. R. B. ATKINSON, Brit. J. Child. Dis. **37**:35 (Jan.-March) 1940.

This article refers to 30 published cases of Lederer's anemia occurring in children and 29 of the same condition occurring in adults. A brief description of the clinical findings and the blood picture is given. There appear to be two types of Lederer's anemia, the acute and the subacute. The diagnosis is based

on the acute onset, the rapid anemia (of the hemolytic type) due to some toxic factor, the exact nature of which is unknown, and the rapid cure resulting from transfusion. Iron is of value in the treatment. LANGMANN, New York.

PERICARDIAL EFFUSION IN INFANCY. MAURICE DAVIDSON, Brit. J. Tuberc. **33**:138 (July) 1939.

An otherwise healthy boy of 2½ years suffered from increased dyspnea on exertion. He was cyanosed at birth, and there was some difficulty in establishing respiration. After a few early illnesses and troubles related to feeding he progressed normally. On exertion, however, e. g., while he was taking the bottle and later, when he became increasingly active, there were some dyspnea and pallor but no cyanosis. The dyspnea had increased, although the child appeared otherwise healthy, active and energetic. Examination of the chest revealed an area of dulness anteriorly, with diminished breath sounds. The heart sounds were normal. There was an area of distended veins below the left clavicle. The radiologist's report was "? heart, ? neoplasm." A tentative diagnosis of mediastinal tumor was made. On aspiration 18 ounces (540 cc.) of clear straw-colored fluid was removed. Later a thoracotomy was performed, and no tumor or cyst was found. Since the fluid reaccumulated rapidly, the thorax was opened a second time, and it was then found that the condition was due to a pericardial effusion. A pleuropericardial fistula was established. A few centimeters of fluid was subsequently removed by aspiration, but eventually the fluid seems to have been absorbed and the patient has so far shown no untoward symptoms.

EUGENE H. SMITH, Ogden, Utah.

SPLENOPORTAL THROMBOSES OF CHILDHOOD. MAURICE LAMY, Arch. de méd. d. enf. **43**:5 (Jan.-Feb.) 1940.

Among splenomegalies, one type deserves particular attention. It is characterized essentially by two symptoms, recurring hemorrhages from the gastrointestinal tract and chronic enlargement of the spleen, and it represents a special anatomic lesion, thrombosis of the splenic vein.

Kleinschmidt, in 1916, reported the first instance of this disease. A number of American and European clinicians have since reported cases. The author presents in detail observations on 4 children ranging in age from 10 to 14 years. In each case the cardinal syndrome of gastric hemorrhage and splenomegaly dominated the picture. The sole means of treatment appears to be prompt splenectomy.

AMESSE, Denver.

A FURTHER CONTRIBUTION ON THE ANEMIA OF LEDERER. A. COLARIZI, Lattante **10**:459 (Dec.) 1939.

Colarizi reports another case of the anemia of Lederer (AM. J. DIS. CHILD. **55**:622, 1938). In a child of 15 months acutely marked anemia of the erythroblastic type developed; there was a rapid response to transfusion therapy. Smears of bone marrow taken by puncture of the tibia at the height of the anemia showed marked megaloblastosis. Injection into rats of gastric juice from the patient failed to result in the principle of Castle, as the reticulocytes were not increased in number. The child died of an intercurrent infection five months after the acute anemia. Autopsy demonstrated complete cure of the anemic process and absence of any alterations suggesting pernicious anemia. HIGGINS, Boston.

CONGENITAL APLASTIC ANEMIA TYPE BENJAMIN. M. ESSER, Ann. pædiat. **154**:305 (March) 1940.

"Description of a case of serious congenital anaemia. The anaemia is characterized by a defective regenerative erythropoetic activity combined with a series of malformations, while the leuco- and thrombocytopoesis remained intact. Pro-

gressiveness in the defection of the erythropoietic function of the bone marrow is unmistakable. This is shown in a bone marrow specimen in an increase of reticulum cells with reduced erythroblastic activity. There is thus an anatomic substratum for this bone marrow disturbance which *Benjamin* believed to be purely functional. As things are this kind of anaemia cannot be influenced therapeutically. Transfusions are only a substitute and no causal treatment."

AUTHOR'S SUMMARY.

ESSENTIAL HYPOCHROMIC ANEMIA IN CHILDHOOD. R. GARSCHE, Ztschr. f. Kinderh. **61**:302 (Oct. 5) 1939.

Achylic chloranemia is seen mainly in women. The author reports the case of a child 1¾ years old, whom he observed for three and one-half years. Increased intestinal motor activity, which interferes with proper absorption of iron, was a prominent feature. Gastric subacidity, dysphagia with esophageal spasm and atrophy of the esophageal mucosa were also present. SIEMSEN, Chicago.

PATHOGENESIS OF OPEN DUCTUS BOTALLI IN ADULTS. F. F. PIAYD, Vrach. delo **20**:151, 1938.

Piayd discusses the anatomy, physiology and etiology of open ductus botalli in adults. An extensive review of the case reports found in the literature is presented, with special reference to those in which the patient has come to autopsy.

The author presents the report of a case of his own in which the diagnosis was confirmed by postmortem examination. This case report is presented in greater detail in a previous article by the same author. BODER, Los Angeles.

HEMATOPOIESIS AND ENDOGENOUS URIC ACID. ROALD OPSAHL, Acta med. Scandinav. **102**:611, 1939.

In 5 cases of pernicious anemia and 2 of posthemorrhagic anemia a considerable increase in the elimination of uric acid was observed during the reticulocyte crisis, while in 1 case of aplastic anemia only a moderate amount of uric acid was found in the urine. This increase in uric acid is endogenous and is probably derived from the disintegrated nuclei of newly formed red blood cells. The present work confirms Krafka's observations on Dalmatian dogs. KAJDI, Baltimore.

Diseases of Nose, Throat and Ear

DEFORMING AND RECURRING POLYPS OF YOUTH. HERNAN I. LAFF, Arch. Otolaryng. **30**:795 (Nov.) 1939.

A case of marked nasal polyposis with resultant external facial deformity in an asthmatic boy aged 15 is presented. The author is of the opinion that the deformity is caused by the effect of gradual pressure of the polypoid tissue on the developing sinal walls. Polyps occurring in childhood, although rare, must be removed early and repeatedly if this is indicated in order to prevent facial deformity, which usually can be repaired by intranasal rhinoplasty; the result can be maintained by adequate control of recurring polyps.

GREENWOOD, Chicago.

TONSILLECTOMY—LOCAL RESULTS AND INFLUENCE OF THE OPERATION ON SURROUNDING TISSUES. EDWARD H. CAMPBELL, Arch. Otolaryng. **30**:863 (Dec.) 1939.

The problem of the recurrence of tonsillar tissue is presented, and statistics are rendered. Factors relative to surgical efficiency are discussed, and the importance of development by the otolaryngologist of a more thorough technic to avoid recurrence and scarring is emphasized. GREENWOOD, Chicago.

DEFECTS IN SPEECH IN RELATION TO DEFECTS IN HEARING. IRVING WILSON VOORHEES, Arch. Otolaryng. **31**:7 (Jan.) 1940.

The author, in discussing the close alliance between speech defects and hearing defects, presents five classifications of such conditions as come under the observation of the otorhinolaryngologist, namely, anatomic defects, such as cleft palate; severe colds and attacks of sinusitis in childhood; speech defects associated with loss of hearing for certain frequencies; congenital or acquired deafness in children, and profound deafness in adults, influencing the quality and intensity of speech.

GREENWOOD, Chicago.

TREATMENT OF LARYNGEAL PAPILLOMA IN CHILDREN WITH ESTROGENIC HORMONE. EDWIN N. BROYLES, Bull. Johns Hopkins Hosp. **66**:319 (May) 1940.

Since papillomas tend to stop growing at or near puberty and since estrogens are known to have the power to change infantile epithelium to epithelium of the adult type, it was thought that local applications of an estrogen to the larynxes of children suffering from papillomas might be beneficial.

Five patients were given weekly applications of amniotin in oil. It was estimated that 0.1 cc. (1,000 international units) of the substance was applied to the larynx at each treatment. The author reports a definitely beneficial effect and thinks that the results of this simple form of treatment are more satisfactory than those obtained in the past.

LYTTLE, New York.

TWO YEARS' EXPERIENCE WITH THE AUDIOMETER IN THE SPRINGFIELD, ILL., SCHOOLS. G. KOEHLER, Illinois M. J. **76**:555 (Dec.) 1939.

During the past two years 6,570 children in the schools of Springfield, Ill., were tested with the 4 B audiometer. Three hundred and four, or 4.6 per cent, had defective hearing as measured by the standard used. In 37,977 hearing tests recently made of school children in Illinois, 13.1 per cent were found to have defective hearing as measured by the standard used. In tests of 1,366 students in the Springfield high school, 6.2 per cent were found to have defective hearing. The results of retests made after one year tend to show that a certain per cent of the hearing deficiencies are evanescent and are recovered from spontaneously.

BARBOUR, Peoria, Ill.

THE RATIONAL TREATMENT OF SINUSITIS IN CHILDREN. JOHN J. SHEA, J. A. M. A. **113**:909 (Sept. 2) 1939.

In treating sinusitis in children, differentiation must be made between symptoms due to infection and those due to allergy. Local treatment is intended to shrink the membranes and allow drainage. Medical treatment is intended to relieve pain and includes the use of sulfanilamide for acute streptococcic infections.

Irrigation may be advisable for both acute and chronic sinusitis. This is done preferably through the natural opening, which may need to be dilated.

Change of climate is a difficult method of treatment because it rarely can be continued long enough.

Regardless of whether the sinuses enter into the production of antibodies, the use of autogenous vaccine modified with an intercurrent vaccine is advantageous for children with persistent sinusitis.

Heat, roentgen therapy and short wave irradiation are valuable in treatment.

Surgical intervention to dilate the ostium or to prepare a window is recommended by the authors for intractable or untreatable infections.

HEERSMA, Kalamazoo, Mich.

BACTEREMIA FOLLOWING TONSILLECTOMY. S. D. ELLIOTT, Lancet **2**:589 (Sept. 9) 1939.

Transient bacteremia was observed in 38 of 100 patients within a few minutes of tonsillectomy. The organisms isolated included Streptococcus pyogenes, Streptococcus viridans, Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus and Corynebacterium. Serologic matches for Str. pyogenes recovered from the blood were isolated from the corresponding tonsils after their removal. In 64 of the 100 cases studied and in 18 additional cases blood for culture was also taken immediately before operation. Of the 82 cases, positive blood cultures were obtained before operation in 7. In 3 of these 7 the postoperative blood culture was positive.

The possible bearing of postoperative bacteremia on the causation of subacute infective endocarditis is discussed.

LANGMANN, New York.

DEFECTIVE HEARING AND NUTRITION IN CHILDREN. PHYLLIS M. TOOKEY KERRIDGE, GWENDOLINE BRIGGS, D. P. JOYCE and JANET HILL, Lancet **2**:781 (Oct. 7) 1939.

Severe deafness is not common among children. In England about 0.1 per cent of children attending public elementary schools are deaf enough for special educational provision.

In a survey of the London children in the schools for the deaf or partially deaf it was found that about half of them were born deaf and about a third were deaf as a result of disease of the middle ear.

All the children tested in this study were between 7 and 14 years of age; one group was chosen from good environments and the other from poor environments. It was found that disease of the middle ear is about four times as common under poor social conditions as it is under good; in the poorest places it may be nearly ten times as common.

As a result of their study the authors feel that probably the most important work on the prevention of deafness will be done by those who are striving to improve the social conditions and in particular the nutrition of the nation.

LANGMANN, New York.

INFLAMMATORY CONDITIONS OF THE UPPER PORTION OF THE RESPIRATORY TRACT. R. A. R. GREEN, M. J. Australia **1**:179 (Feb. 10) 1940.

The lymphoid tissue in the nasopharynx is the most important factor to consider in cases of infection of the upper respiratory tract. In addition to the arrest of infection, these tissues probably aid in developing immunity.

In maintenance of the normal anatomic structure of the nose, methods of feeding are considered important. The work involved in breast feeding tends to produce a lower palatal arch and a roomier nose.

The common cold must always be regarded as a possible forerunner of serious disease. Rest in bed and treatment of the nose until drainage has ceased are important.

In chronic disease of the sinuses infected tonsils play an important role. It is not unlikely that unhealthy conditions in the nose and nasopharynx favor attacks of other diseases, such as poliomyelitis.

The abundant sunlight and available good diet of Australia should make these infections less numerous if these factors are of importance. It is felt that a considerable number of the patients who require hospitalization do so on account of such infections and that there is the possibility that the coastal position, with moist atmosphere, may be one reason for their prevalence.

Adenoids should be removed whenever they are found enlarged, with frequent colds or disease of the middle ear. Tonsils should be left until the age of 5 years unless grossly infected.

TENNEY, Madison, Wis.

BACTERIOLOGY OF THE TONSIL ESPECIALLY IN SCARLET FEVER. KOBYZSKA, CHUDEJOVEJ and HOFFMANN, Bratisl. lék. listy **17**:272 (June) 1937.

The authors were struck by the similarity of cultures of material from the throat of siblings and of children in close contact. A review of the literature is followed by a detailed report on the cultural observations in cases of rheumatism, chorea with and without tonsillitis, scarlet fever, acute and chronic tonsillitis and polyarthritis. The signs and symptoms were no criterion as to the presence of hemolytic streptococci, and the cultural sequence sometimes changed at intervals of several days. In determining the period of isolation for a patient with scarlet fever, both desquamation and cultural observations must be considered. Among 69 patients with scarlet fever, the bacteriologic findings of 6 became normal in three weeks, of 5 in four weeks, of 11 in five weeks, of 34 in six weeks and of 13 in seven weeks. In a considerable percentage of cases the period of desquamation and that of positive cultures were synchronous. Convalescent patients and those with the disease in the early stage should be separated to avoid reinfection. Reinfection with other organisms, such as staphylococci, is an important factor, because of lowered tissue resistance resulting from the primary streptococcic infection.

STULIK, Chicago.

Diseases of Lungs, Pleura and Mediastinum

A PRELIMINARY REPORT OF SULFANILAMIDE AND AMIDOPYRINE THERAPY OF PNEUMONIA. C. L. THENEBE, M. S. HIRSHBERG and A. BOBROW, Arch. Pediat. **56**:795 (Dec.) 1939.

This type of therapy was used in 20 cases of pneumonia, with gratifying results.

ORR, Buffalo.

OIL ASPIRATION PNEUMONIA AND PNEUMOLIPOIDOSIS. PHILIP G. C. BISHOP, Ann. Int. Med. **13**:1327 (Feb.) 1940.

A review of the literature revealed 136 cases. Pneumolipoidosis is the term suggested for conditions in which pneumonia due to bacterial infection is absent. A complete description of the disease is given, with excellent roentgenograms and photomicrographs of sections of lung tissue, showing various pathologic aspects of the condition. Four cases are reported. The bibliography contains 107 references.

READING, Galveston, Texas.

THE ETIOLOGIC DIAGNOSIS OF PNEUMONIA IN CHILDREN BY RAPID TYPING OF NASAL CULTURES. FRANKLIN D. POOLE and MILDRED D. FOUSEK, J. A. M. A. **113**:1854 (Nov. 18) 1939.

Complete typing of nasal cultures for suspected pneumonias in children was made in four to six hours by the technic described. The results of nasal and pharyngeal cultures checked fairly well with those of cultures made from pleural exudates and from material discharged from the ear.

HEERSMA, Kalamazoo, Mich.

THE SULFAPYRIDINE TREATMENT OF PNEUMONIA IN CHILDREN. CHARLES HENDEE SMITH and ROSA LEE NEMIR, J. A. M. A. **113**:1857 (Nov. 18) 1939.

Ninety-three patients were treated for pneumonia with sulfapyridine. Twenty-nine were under 2 years of age, and 11 of these had bronchopneumonia.

Seventy-nine others had lobar pneumonia. In cases of bronchopneumonia the disease did not seem to be affected by the treatment, and 4 of the patients died.

In 74 of the 79 cases of lobar pneumonia a crisis occurred in eighteen to twenty-four hours. A crisis occurred in less than forty-eight hours in the remaining 5 cases. One death occurred, from pyopneumothorax.

The authors early began to give smaller doses and shorter courses than are usually recommended, totaling less than 4 to 6 Gm. over two to three days. Nausea was the most frequent problem, and some other reactions and results are described. Typing was significant as to prognosis.

HEERSMA, Kalamazoo, Mich.

STAPHYLOCOCCUS PNEUMONIA: A CLINICAL, PATHOLOGIC, AND BACTERIOLOGIC STUDY. ABRAM KANOF, BENJAMIN KRAMER and MOSES CARNES, J. Pediat. **14**:712 (June) 1939.

This report presents an analysis of 37 cases of pneumonia in which the staphylococcus was the etiologic agent. The patients were classified into two groups: (1) patients having primary staphylococcic pneumonia and (2) patients with secondary staphylococcic pneumonia in the course of staphylococcic sepsis. Twenty-five of the patients were in the first group and 12 in the second. Cultures of the blood of all those with the secondary type of disease gave positive results, and only 1 of the 25 patients in the first group had a positive culture during life. In 80 per cent of the patients in group 1 the disease occurred during the winter or the early spring, whereas in 60 per cent of those in group 2 the onset occurred during the summer. In group 1 the number of boys and that of girls were equal; however, twice as many boys as girls suffered from secondary staphylococcic pneumonia. Primary staphylococcic pneumonia occurred more often in infants and young children, whereas the secondary form was more frequent in children over 5 years. Empyema occurred often in both groups, in 87 per cent of group 1 and in 58 per cent of group 2. Empyema appeared to develop early. Infection of the upper respiratory tract was present in 80 per cent of the patients having primary pneumonia but in only 33 per cent of those in whom the disease was secondary. In none of the patients in group 1 did any pyogenic localization occur outside the respiratory tract. In group 2, osteomyelitis developed in 5 patients, multiple cutaneous infections in 7, metastatic foci in the peritoneum in 2 and abscesses in the kidneys in 2. The mortality rate among the patients with primary pneumonia was 65 per cent, and among those in whom the disease was secondary, 83 per cent. Infants under 1 year of age had the highest mortality. In group 1 the pathologic change was confined essentially to the lungs. In group 2, in addition to the metastatic abscesses in the lungs, abscesses were found in many other organs, and nearly all the patients in group 2 had osteomyelitis.

RAUH, Cincinnati.

THE SIGNIFICANCE OF TYPE 14 PNEUMOCOCCUS INFECTION AND THE THERAPEUTIC VALUE OF SPECIFIC RABBIT SERUM FOR THIS TYPE OF PNEUMONIA IN INFANTS AND CHILDREN. EDWARD C. CURNEN, New England J. Med. **221**:725 (Nov. 9) 1939.

The purpose of this paper is to direct attention to the frequency, age incidence and pathogenicity of the type XIV pneumococcus as it occurs in patients under 12 years of age and to show the results obtained at the Infants' and Children's Hospitals (Boston) in the treatment of this type of pneumonia with concentrated specific rabbit serum.

Pneumococcus type XIV, obtained from 120, or 20 per cent, of all the patients and from 104, or 25 per cent, of those with pneumonia, was the most frequent single type encountered and was the dominant pneumococcic agent of pneumonia.

The type XIV pneumococcus showed an extraordinarily selective distribution and pathogenicity among infants and young children of preschool age, yielding its dominance among older children to the type I pneumococcus.

Pneumonia due to the type XIV pneumococcus was clinically indistinguishable from that due to other organisms.

For every patient receiving serum, treatment was carried out by the intravenous route.

According to the schedule of treatment gradually formulated, an initial small injection of from 0.5 to 1 cc. of serum diluted 1:5 or 1:10 with physiologic solution of sodium chloride was followed after intervals of two hours by larger amounts (from 4.5 cc. to 10 cc.) of serum similarly diluted, provided no reactions had supervened. With concentrated serum of high potency, it was usually possible to administer an effective therapeutic dose in two injections.

Antipyretic drugs were omitted during the administration of serum in order to avoid confusion of therapeutic effects.

Reactions to serum occurred in 13 of the 34 patients treated.

Thirty-one of the 34 patients who received concentrated antipneumococcus type XIV rabbit serum appeared to be improved by this form of therapy.

For the 31 patients who were benefited, 9 cc. of serum, or 36,000 units of antibody, was the average dose employed.

The failure of serum therapy was attributable in 2 cases to the presence of infection with other types of pneumococci and in 1 case to the presence of a purulent focus of infection (empyema) at the time treatment was started, late in the course of the disease.

The long duration of acute illness in the untreated patients was accounted for in most cases not by complications but by continuation of the pneumonic process, with spread to other areas or failure to terminate by lysis or crisis.

Complications, with the exception of otitis media, which occurred in 66 per cent of all the cases, were relatively uncommon.

Serious complications, although infrequent, almost invariably proved fatal in patients who were not treated with serum and did not occur in those receiving concentrated serum, save in the 2 patients who had empyema at the time antipneumococcus type XIV serum was first administered.

Among the 34 patients who received concentrated rabbit serum, 22 of whom were infants under 2 years of age, there were no fatalities.

GENGENBACH, Denver.

TWO CASES OF ENCEPHALITIS IN THE COURSE OF PNEUMONIA IN A CHILD. P. LEREBOULLET, M. LELONG and J. GUILLEMIN, Arch. de méd. d. enf. **43**:26 (Jan.-Feb.) 1940.

Numerous cases have been reported of encephalitis occurring during or after eruptive fevers in children, but the occurrence of this secondary infection in association with pulmonary diseases is rare. Hempelmann, in the epidemic of 1931, found in a series of 38 but 1 case of encephalitis complicating pneumonia. Comby, in 1933, and Desmarquest, in 1934, likewise could report but 1 each in this category. Two further cases are offered by the authors; in each the patient was a child of 4 years.

AMESSE, Denver.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

CATARRHAL ICTERUS. JOSEPH SCHWARTZMAN and ANTHONY MAFFIA, Arch. Pediat. **57**:181 (March) 1940.

Thirty-five cases of the sporadic condition are reviewed with reference to seasonal occurrence, sex, age, symptoms and laboratory findings.

Most of the patients were between the ages of 3 and 11 years, and the disease in most instances was ushered in by a gastrointestinal syndrome and in 10 cases by an infection of the upper respiratory tract. The symptoms at the onset were fever, anorexia, vomiting and abdominal pain, followed by enlargement of the liver

and occasionally of the spleen. With the onset of jaundice the gastrointestinal symptoms and the fever usually subsided, and recovery was uneventful.

Diet had little or no influence on the course of the illness. ORR, Buffalo.

PRIMARY PERITONITIS IN INFANTS AND CHILDREN. WILLIAM E. LADD, THOMAS W. BOTSFORD and EDWARD C. CURNEN, J. A. M. A. **113**:1455 (Oct. 14) 1939.

Sixty-seven cases of primary peritonitis in infants and children are reported. In 47 the disease was caused by hemolytic streptococci and in 20 by pneumococci. All the conditions were probably hematogenous and usually followed infections of the respiratory tract. Nephrosis predisposed to pneumococcic peritonitis.

The great importance of early diagnosis and specific therapy is evidenced by a reduction in mortality rates in the streptococcic group from 72 per cent to 28.5 per cent and in the pneumococcic group from 83.3 per cent to 12.5 per cent. The diagnosis was made certain by blood culture and by examination of the peritoneal fluid obtained immediately by incision and drainage.

Treatment was by use of sulfanilamide, sulfapyridine or type-specific serum, with fluid given intravenously and subcutaneously, with blood transfusions and when necessary with gastric siphonage and oxygen.

HEERSMA, Kalamazoo, Mich.

CYSTIC FIBROSIS OF THE PANCREAS, VITAMIN A DEFICIENCY, AND BRONCHIECTASIS. D. H. ANDERSON, J. Pediat. **15**:763 (Dec.) 1939.

The disease entity, cystic fibrosis of the pancreas, is not rare but is infrequently recognized. The onset of symptoms occurs in the neonatal period. The symptoms are: large foul stools, failure to gain weight in the presence of a good appetite and adequate food, a tendency to repeated or chronic respiratory infection and a history of similar disease in the siblings. Bronchiectasis and vitamin A deficiency, especially xerophthalmia, are such frequent symptoms of the disease that Anderson feels the presence of either condition in infancy should arouse suspicion of the presence of cystic fibrosis of the pancreas. The diagnosis may be proved by an assay of pancreatic enzymes. No pancreatic trypsin or lipase will be found in the duodenal juice. A celiac diet modified by the use of whole milk with pancreatin, adequate vitamin A and a diet 20 to 40 per cent more than the estimated caloric requirement are the therapeutic suggestion. RAUH, Cincinnati.

ACUTE INTUSSUSCEPTION WITH INTERMITTENT SPONTANEOUS REDUCTION AND RECURRENCE. R. F. ZEIGLER JR., J. South Carolina M. A. **35**:217 (Sept.) 1939.

The title of the report explains the case of a Negro boy of 3 years. The intussusception was reduced on operation, and further occurrence was prevented by appendectomy and cecopexy. WESTON JR., Columbia, S. C.

DOUBLE INTUSSUSCEPTION. E. B. FINE, J. South Carolina M. A. **35**:227, 1939.

Intussusception occurred, following an attack of diarrhea, in a white boy 1½ years of age. He proved to have Meckel's diverticulum. The diverticulum was removed and the stump inverted by the usual procedure. The appendix was not removed, nor were the intestines anchored to the peritoneum. There was an uneventful recovery. WESTON JR., Columbia, S. C.

RESTRICTED DIET IN THE TREATMENT OF GASTROENTERITIS IN INFANTS. H. GRENET, P. ISAAC-GEORGES and A. WIMPHEN, Bull. Soc. pédiat. de Paris **37**:253 (May) 1939.

Infants who had become dehydrated as a result of intestinal indigestion were given nothing by mouth for twelve to twenty-four hours, and fluids were adminis-

tered parenterally. Vomiting and diarrhea ceased, and the diet was gradually built up. The results are believed to be better than those obtained when ingestion of fluids is not discontinued.

BENJAMIN, Montreal, Canada.

CELIAC DISEASE. G. L. HALLEZ, Progrès méd. **68**:61 (Jan. 20) 1940.

In addition to the usual measures employed in the management of celiac disease the author emphasizes the particular value of the vitamins in the B_2 or G complex.

LESLIE, Evanston, Ill.

HERNIAS IN INFANTS AND YOUNG CHILDREN. S. SZOMBATI, Orvosi hetil. **83**:829 (Aug. 26) 1939.

Szombati reports 562 operations for hernia done on children up to 4 years of age. Almost all the hernias were congenital. The inguinal hernias were much more common in boys than in girls, the rates being 91.10 per cent for boys as compared with 8.90 per cent for girls. Sixty-seven patients were operated on in infancy and all made prompt recovery. Inguinal hernias should be operated on in infancy only when incarcerated or so big that the danger of incarceration threatens. Before the operation, reposition should invariably be attempted, always with the patient in narcosis. In no case of incarceration was resection of the intestines necessary, for necrosis was never present. Operation on inguinal hernias in infants is easy, requiring only ten to fifteen minutes. Thirteen patients were operated on because of cryptorchidism; in 2 the testicles were strangulated, so that they had to be removed. Szombati thinks that the best age for transplantation of the testicles is between 2 and 6 years. Thirty-three patients were operated on for umbilical hernia. Two patients with amniotic hernia were operated on two hours after birth; 1 died. Apart from this patient, of all his 562 patients Szombati lost only 1, a 14 month old boy, who died of pneumonia.

GÖTTCHE, Budapest, Hungary.

FLUCTUATION OF LACTIC ACID IN THE GASTRIC JUICE DURING VARIOUS SECRETORY GASTRIC STATES. G. M. BOGDANOVA and E. B. BANTIN, Vrach. delo **21**:213, 1939.

The authors point out that the question of the presence of lactic acid in the gastric juice has been the subject of various investigations and that the opinions on the significance and origin of lactic acid in the gastric juice are still divided.

The amount of lactic acid in the gastric juice was studied by the authors in observations on dogs as well as on human beings, under various conditions, such as those following fasting, intake of meat and administration of caffeine. The gastric juice was tested for total acidity and for free hydrochloric and lactic acid. The authors' conclusions were as follows:

1. Lactic acid may be found constantly in gastric juice under normal as well as abnormal gastric conditions.

2. The amount of lactic acid in gastric juice is considerably higher after breakfast than after fasting.

3. The content of lactic acid in the gastric juice is lower after administration of meat than after administration of caffeine.

4. The amount of lactic acid in the gastric juice varies in inverse proportion to the content of hydrochloric acid, i. e., when the acidity rises the content of lactic acid falls.

BODER, Los Angeles.

Nervous Diseases

PNEUMOCOCCUS MENINGITIS—RECOVERY FROM SPECIFIC TREATMENT. DEWITT H. SHERMAN, Arch. Pediat. **57**:112 (Feb.) 1940.

A boy 8½ years old was successfully treated for pneumococcic meningitis with the combined use of serum and sulfapyridine. The meningitis was due to pneumococcus type XXI. The spinal fluid became sterile on the ninth day of treatment. Deafness developed as a result of the disease. There were no other sequelae.

ORR, Buffalo.

INFLUENZAL MENINGITIS WITH BACTEREMIA TREATED WITH SULFAPYRIDINE: RECOVERY. TOM R. HAMILTON and FRANK C. NEFF, J. A. M. A. **113**:1123 (Sept. 16) 1939.

The disease in a 2 year old child responded well to treatment with sulfapyridine within a few days after the onset and after a recurrence. The complete case report is given.

HEERSMA, Kalamazoo, Mich.

STUDIES ON HERPES SIMPLEX ENCEPHALITIS IN RABBITS: I. THE THERAPEUTIC EFFECT OF VITAMIN C, SULPHANILAMIDE AND PITRESSIN. J. FLEXNER, M. CHASSIN and I. S. WRIGHT, J. Infect. Dis. **66**:30 (Jan.-Feb.) 1940.

Vitamin C, pitressin and sulfanilamide are worthless as therapeutic agents in cases of herpes simplex encephalitis in rabbits. The incidence of paralysis was not decreased by these agents.

TOOMEY, Cleveland.

NARCOLEPSY. PETER G. DANIS, J. Pediat. **15**:103 (July) 1939.

A case of narcolepsy in an 8 year old white girl is presented. Treatment with thyroid and pituitary preparations caused no alleviation of symptoms. Prompt relief of symptoms, however, was achieved by the use of ephedrine sulfate. Therapy was continued for a year, after which time the child became symptom free. A recurrence of symptoms occurred six months after discontinuance of the administration of ephedrine sulfate. The patient was again treated, for a month, and became free of symptoms.

RAUH, Cincinnati.

THE SYNDROME OF HYDROMICROCEPHALY. JOSEPH E. MCCLELLAND, J. Pediat. **16**:36 (Jan.) 1940.

In a study of 142 pediatric neurologic conditions 13 cases of hydromicrocephaly were encountered. In all there were dilated ventricles and early closure of the fontanel. Frequent observations were spasticity, mental deterioration and defective vision. Most of the authors who have reported similar cases regard hydromicrocephaly as a prenatal defect. McClelland concurs in this view, provided cerebral anoxia at birth can be ruled out.

RAUH, Cincinnati.

RECOVERY FROM SALMONELLA (PANAMA) MENINGITIS IN AN INFANT TREATED WITH SULFAPYRIDINE. CHRIS P. KATSAMPES and WILLIAM L. BRADFORD, J. Pediat. **16**:79 (Jan.) 1940.

Katsampes and Bradford report the case of an infant suffering from enteritis and meningitis. The organism Salmonella (Panama) was isolated from the stool, the blood stream and the spinal fluid. The infant recovered from the first attack, and a second attack of meningitis due to this organism developed six weeks later. The patient subsequently recovered. Therapy consisted of repeated lumbar punctures, blood transfusion and the administration of sulfapyridine.

RAUH, Cincinnati.

"INFLUENZAL" MENINGITIS TREATED WITH M & B 693. E. H. ROCHE and J. E. CAUGHEY, Lancet **2**:635 (Sept. 16) 1939.

This is a report of the recovery of 2 consecutively observed patients, aged 17 months and 12 years respectively. Bacillus influenzae was cultured from the spinal fluid of both patients. The younger child received the drug orally for the first two days and then (because of vomiting) intramuscularly and subcutaneously in an oily suspension. Blood transfusions were given twice in both cases.

LANGMANN, New York.

NEUROFIBROMATOSIS WITH SYNDROME OF MEDIASTINAL COMPRESSION AND ARAN-DUCHENN HAND. G. BOUDET, J. BALMÈS and J. BARNAY, Bull. Soc. pédiat. de Paris **37**:198 (April) 1939.

A boy 9 years old complained of pain in the left side of the chest. He was emaciated. There was a deformity of the chest, with dorsal scoliosis. The left hand showed atrophy of the interosseous muscles as well as of the hypothenar and thenar eminences. The left eye revealed miosis, ptosis and enophthalmos (Horner's syndrome). Roentgen examination demonstrated density of the apex of the right lung and the mediastinum, periosteal thickening of the metacarpal bones and a deformity of some vertebrae. There were some areas of cutaneous pigmentation. A biopsy specimen of a subcutaneous nodule from the left axilla was diagnosed microscopically as neurofibromatous tissue.

BENJAMIN, Montreal, Canada.

TUBEROUS SCLEROSIS OF MALIGNANT TYPE. L. MARCHAND, M. BRISSOT and J. MAILLEFER, Encéphale **1**:57, 1939.

The authors present a case of a malignant type of tuberous sclerosis in a 6 year old male idiot with epilepsy. The mother and both maternal grandparents were mentally deficient. A 4 year old brother was markedly retarded and epileptic and had adenoma sebaceum of the face. The patient had numerous tumors of the face, forehead and scalp and two small tumors on the trunk. He died after rapidly progressive cachexia. A few days before death, a soft subcutaneous tumor appeared in the cervical region. Both cerebral hemispheres contained multiple cortical patches of tuberous sclerosis. The walls of both lateral ventricles consisted of a soft whitish tissue containing small hemorrhages. In the left hemisphere the choroid plexus contained numerous miliary nodules. The caudal portion of the right thalamus contained a tumor the size of a nut. The brain stem and cerebellum showed no gross lesions. The heart contained multiple whitish masses in the myocardium; there were multiple renal tumors. Microscopically, the cerebral cortex, in addition to the tubers, presented gliosis, demyelination and monstrous ganglion cells and astrocytes. The ganglion cells were few and atypically formed and contained sparse neurofibrils. The subependymal tissue showed diffuse proliferation of glia cells, many of which were monstrous and multinucleated. The thalamus contained an astrocytoma with large fusiform cells. In the right restiform body was a small nodule of cytoplasmic glia. The tumor of the choroid plexus was a meningioma made up of fusiform cells, between which were collagen and thin-walled capillaries. In the deepest portion of the molecular layer of the cerebellum were multiple small gliomatous nodules made up of astrocytes with few fibrils. The tumor of the neck was identical in structure with the astrocytoma of the thalamus. There were gigantic, polymorphous stellate cells, often arranged about blood vessels. The renal tumors were made up of granular cells in a network of reticulin. They had some features of the epithelial type of meningioma and of peripheral glioma. The myocardial tumors resembled rhabdomyoma but contained cells of a sympathoblastic type. These tumors, while they correspond to the features of rhabdomyoma, seem to be

of sympathetic, not of muscular, origin. The tumors of the skin were composed of fibroblasts, believed to be altered Schwann cells, and contained excessive collagen in the cutis. Tuberous sclerosis comprises two types of processes: (1) a diffuse growth of neuroglia cells without compression or destruction of other elements and (2) the formation of well defined gliomas, with malignant evolution. All these particulars indicate the close relation between neurofibromatosis and tuberous sclerosis, both neurorectodermal, hereditary diseases, in which hyperplastic and neoplastic gliomatous lesions of the brain are observed. There are cases in which, even after histologic study, it is difficult to determine with which of these diseases one is dealing.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

ETIOLOGIC DIAGNOSIS OF PARALYSIS IN CHILDREN. L. BABONNEIX, Paris méd. **2**:230 (Oct. 7-14) 1939.

Six cases are presented in which the diagnosis of poliomyelitis was considered but finally discarded. In 1 patient the large amount of albumin with the absence of cells in the spinal fluid helped to establish the diagnosis of radiculoneuritis of the Guillain-Barré type. In another, myoclonus, salivation and the parkinsonian phenomena pointed to epidemic encephalitis. Blockage of the spinal canal in a third led to the injection of iodized poppyseed oil and the operative finding of acute arachnoiditis. The conditions in the other cases, because of the complex picture, were considered to be encephalitides of undetermined origin.

LESLIE, Evanston.

ENCEPHALITIS AND ENCEPHALOPATHIES WITH REGRESSIVE EVOLUTION IN CHILDREN; SEMEIOLOGIC ASPECTS. AUGUSTE TOURNAY, Paris méd. **2**:236 (Oct. 7-14) 1939.

The author has had experience with 100 cases. His reflections and comments on the semeiologic aspects are not particularly clarifying, although they might prove valuable to one who has had considerable experience in this field.

LESLIE, Evanston.

PRECOCIOUS MACROGENITOSOMIA (PELLIZZI SYNDROME) IS NOT OF PINEAL ORIGIN. M. SCHACHTER, Paris méd. **2**:244 (Oct. 21-28) 1939.

An excellent study and review of the literature on the subject of macrogenitosomia are presented, from which Schachter easily shows that the pineal body per se has nothing to do with the syndrome under consideration. The syndrome may be associated with various types of intracranial tumors, encephalitic infections or congenital malformations of the superior nervous centers or may be seen as a heredofamilial condition. The author feels that the essential injury is to the mesodiencephalon; that this may be either primary or secondary, and that it may occur either with or without hydrocephalus.

LESLIE, Evanston.

RECURRENT MENINGEAL HEMORRHAGES IN A CHILD. G. L. HALLEZ, Paris méd. **2**:275 (Nov. 18) 1939.

A case is reported in which there were recurrent meningeal hemorrhages. The first occurred at the time of birth, the second during the eighth year, the third and the fourth during the ninth year, the fifth at 11 years of age and another at 12 years. Syphilis and blood dyscrasias were ruled out. Abnormal fragility of the capillaries in the arachnoid space was postulated. There were no residual symptoms, and at the age of 13 years the child was in excellent condition.

LESLIE, Evanston.

INFLAMMATORY SCLEROSIS OF THE WHITE MATTER OF THE HEMISPHERES. LUDO VAN BOGAERT and JACQUES DE BUSSCHER, Rev. neurol. **71**:679, 1939.

Van Bogaert and de Busscher report the case of a boy aged 8 years who had been the first pupil in his class and who began to fail in schoolwork, particularly in arithmetic. His writing became disordered and incorrect. He became coarse and brutal, had nocturnal terrors, talked at night and seemed to have hallucinations. His writing became more impaired, with omission of letters or reduplication of syllables. Finally, he could not read except in a mirror. Other signs of extensive and severe visual dysgnosia developed, such as taking strangers in the street for his father, confusion of his possessions with those of his fellow pupils, searching vainly at table for familiar objects and inability to copy except by servile reproduction of the words, without comprehending them. Finally, after four months, his parents believed him to have become an idiot and took him to a physician. Examination revealed bilateral papilledema, a cracked pot sound on percussion of the skull, slight, questionable right hemiparesis and clumsy gait with occasional falling. The reflexes were all normal. In addition to visual agnosia, there were aprexia and advanced aphasia of the semantic type. There were attacks of pallor, opisthotonos and generalized rigidity, recalling Jackson's cerebellar fits. There was no evidence of syphilis or other infection. Roentgenograms of the skull showed mottling characteristic of intracranial pressure. The symptoms increased. Vomiting, headache and conjugate deviation of the head and eyes to the right appeared. A diagnosis of glioma of the left parieto-occipital region was made. Craniotomy revealed a tense and nonpulsating dura, but no tumor. Death with hyperthermia followed. There was diffuse, moderate demyelination of the cerebral and cerebellar white matter, most marked in the parieto-occipital region, accompanied by diffuse gliosis. The latter was more extensive than the loss of myelin. In the white matter of both hemispheres were multiple, focal, perivascular infiltrations with lymphocytes and plasma cells. The cortex had inflammatory nodules consisting of similar infiltrations, together with neuroglial and microglial proliferation, formation of rod cells, satellitosis and destruction of ganglion cells in layers II, III, V and VI. The overlying leptomeninx showed severe infiltration with lymphocytes and plasma cells. These lesions were particularly severe in the cunei, the precunei and the superior temporal and interparietal sulci. The central gray nuclei, the substantia nigra, the substantia reticulata of the brain stem and the nucleus of the corpus restiforme showed similar lesions. The pons showed diffuse marginal gliosis. The topographic distribution of the lesions was characteristic of diffuse sclerosis, the site of greatest intensity being in the occipital pole, lateral to the optic radiations. A peculiar feature was the intense inflammation of the gray as well as of the white matter, which could not be explained as reactive since no products of disintegration were seen in the inflamed areas. The condition is classified as inflammatory sclerosis of the white matter of Spielmeyer, and is believed to be caused by an infection of unknown nature.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

A PECULIAR TYPE OF CONGENITAL HYDROCEPHALUS DUE TO HYPERTROPHY OF THE CHOROID PLEXUSES OF THE LATERAL VENTRICLES. S. FOLENA, Riv. di clin. pediat. **38**:93 (Feb.) 1940.

A case report is given of a child who first showed enlargement of the head at 1 month of age and died at 26 months, of erysipelas. Marked hypertrophy of the choroid plexuses of the lateral ventricles, in the absence of other anatomic reasons for the hydrocephalus, offers the probable basis for the condition.

HIGGINS, Boston.

ASTROCYTOMAS OF THE MEDULLA OBLONGATA, PONS AND PEDUNCLE. O. FOERSTER and O. GAGEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **166**:497 (July) 1939.

Foerster and Gagel report 12 cases of astrocytoma of the brain stem, 7 of which were in males and 5 in females. Five of the patients were in the first decade of life; 1 was 2 years of age. There was 1 patient each in the second and the third decade; 3 were in the fourth, and 2 in the fifth decade. The average duration of illness in the 10 cases in which such information was obtained was three years and three months; the shortest period was three and one-half months, and the longest, fourteen years and two months.

The clinical picture was recorded in 10 of the cases. In 1 case the cranial nerves and long tracts were spared. The presenting symptom was frontal headache, of two years' duration. This was due to internal hydrocephalus resulting from the protrusion of the tumor into the fourth ventricle. In most of the other cases there was alternating hemiplegia, with cranial nerve involvement on one side and hemiplegia on the other. In 1 case of pontile tumor cerebellar fits were noted. Thalamic or central pain was recorded in 1 case. Nerve deafness due to unilateral involvement of the cochlear nuclei was present. Contractures of the facial muscles were seen. In 1 case the onset of the illness was with a facial tic. In 2 cases the symptoms appeared soon after trauma to the head. In 1 case there was marked improvement for six and one-half years.

In 4 cases the tumors were clearly circumscribed and in 4 others infiltrating. The infiltrating tumors were encountered mainly in older patients, except in 1 case in which the anomaly occurred in a boy aged 11. There was no histologic difference between the tumors of younger and those of older patients. The circumscribed protoplasmic astrocytomas differed in no way from similar tumors more commonly seen in the cerebral hemispheres and cerebellum. The circumscribed fibrillary astrocytomas in the brain stem, however, were more cystic than similar tumors in the basal ganglions, thalamus or cerebral hemispheres. The authors comment on the frequency of piloidal astrocytes.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

VITAMIN B IN TREATMENT OF DISEASES OF NERVOUS SYSTEM IN CHILDREN. P. KISS, Orvosi hetil. **83**:511 (May 27) 1939.

The author gave vitamin B_1 in large doses and for a longer period for diseases of the nervous system (postdiphtheritic paralysis, poliomyelitis, encephalitis, chorea minor). In spite of the fact that the effect cannot be regarded as specific, the results were in some cases so good that the author expresses the belief that vitamin B_1 should be given besides the other regular treatment to patients with the aforementioned diseases of the nervous system. GÖTTCHE, Budapest, Hungary.

Psychology and Psychiatry

PHANTASY IN MAL-ADJUSTED CHILDREN AS OBSERVED IN THREE CASES AT THE SOUTHARD SCHOOL. EUGENE EISNER, Bull. Menninger Clin. **3**:27 (Jan.) 1939.

The fantasies and backgrounds of 3 children are discussed. One child had had a fractured skull; the other 2 compared unfavorably with other members of their families. In all instances the fantasies were of a nature to make the child seem more important to himself and, according to his judgment, to others. The author is particularly interested in the appearance of loss and hate motives and in the erotic (termed constructive) and the aggressive (termed destructive) elements.

LESLIE, Evanston, Ill.

POSSIBILITY AND ORGANIZATION OF PREVENTIVE NEUROPSYCHIATRIC PROCEDURES IN EARLY CHILDHOOD. P. BRUSA, Lattante **11**:69 (March) 1940.

This is a lecture covering the field of preventive neuropsychiatric practice among young children.

HIGGINS, Boston.

CHILDHOOD AND THE CINEMA. DANTE COSTA, Bol. Inst. internac. am. de protec. a la infancia **13**:703 (April) 1940.

The author advises regulating the attendance of children at moving pictures. Attendance of children younger than 6 years should be forbidden; the others might go to special performances, but never at night.

FROM EDITOR'S SUMMARY.

STUDY OF EMOTIONAL FEELINGS IN THE CHILD. JOSÉ FLORES MUÑOZ, Bol. Inst. internac. am. de protec. a la infancia **13**:790 (April) 1940.

The author summarizes a few general ideas about certain emotional problems and about the behavior of some children. In all children there is a latent sense of fear—fear of exhibiting a physical defect, horror of speaking before other persons and a certain fear in intercourse with playfellows. The adequate treatment for such conditions is based on the comprehensive and affectionate attitude of parents and teachers.

FROM EDITOR'S SUMMARY.

LYING IN CHILDREN. JOSÉ FLORES MUÑOZ, Bol. Inst. internac. am. de protec. a la infancia **13**:820 (April) 1940.

The author studies the influence of environment on innate sincerity in infancy; the child from a tender age becomes aware of the fact that he lives in a false environment; he hears lies at home, in the school, in the street. Nevertheless the child is compelled to tell the truth.

Imagination, dreams and incomplete perceptions produce mistakes, which should not be called lies. Actual falsification may be indulged in to produce tranquillity and at least temporary satisfaction.

From the educational point of view the author studies how to avoid lying and how to correct the evil if it is produced; he describes and analyzes several cases, establishing that physical punishment should not be employed. Frequently advantage should be taken of the different intellectual and emotional stages through which the child is passing. Between the ages of 10 and 12 he wants to be strong and brave; truth then must be united to courage and the development of physical strength. In adolescence truth should be associated with esthetics, for youth is sensitive to beauty and purity, and the lie, ugly and sinful, is disagreeable to the mind. Moral greatness lies in telling the truth.

FROM EDITOR'S SUMMARY.

SEXUALITY IN CHILDREN. E. STERN, Ann. pædiat. **155**:36 (April) 1940.

This paper gives the results of an inquiry about infantile sexuality and sexual education. The replies of the collaborators (chiefly pupils of a senior grammar school) show that the child manifests from the fifth year of his life a distinct sexual activity, about the nature of which there cannot be any doubt. There is found once more in the replies all the facts revealed by Freud's psychoanalysis. These manifestations, often contested or taken as expressions of a psychoneurotic disturbance, seem to be perfectly normal. A proper sexual education exists only in few cases. The greater number of the subjects regret that their parents took so little trouble to educate them in this respect. FROM AUTHOR'S SUMMARY.

Diseases of the Genitourinary Tract

THE DIAGNOSIS AND TREATMENT OF URINARY INFECTIONS IN CHILDREN. J. D. YOUMAN, New Orleans M. & S. J. **92**:425 (Feb.) 1940.

The importance of closer cooperation between pediatricians and urologists is stressed. It is urged that patients unresponsive to four weeks of medical treatment be referred to a urologist for complete urologic investigation. In this way obstructive anomalies, calculi and tumors will often be found. BERKLEY, Los Angeles.

TONSILLECTOMY AND NEPHRITIS OF CHILDHOOD. R. S. ILLINGWORTH, Lancet **2**:1013 (Nov. 11) 1939.

Opinions on the value of tonsillectomy in cases of nephritis are many and varied.

Of 301 patients admitted to the Hospital for Sick Children in the last eleven years for acute nephritis, 61 (20.2 per cent) had undergone tonsillectomy some months or years previously.

The conclusion reached is that tonsillectomy does not prevent nephritis but may predispose to it, that it does not cure nephritis or prevent it from progressing to a chronic stage and that it may cause nephritis. LANGMANN, New York.

ETIOLOGY OF RENAL DWARFISM: FAMILIAL DWARFISM AND DWARFISM DUE TO INTOXICATION DURING GESTATION. B. WEILL HALLÉ, A. ABAZA and MEUNIER, Bull. Soc. pédiat. de Paris **37**:266 (May) 1939.

Three children of one family were afflicted with renal dwarfism. One of them apparently had shown the condition since birth; the mother had suffered from toxemia during pregnancy with this child. Renal damage was present in all the children. One, who was examined post mortem, showed the usual renal atrophy and sclerosis. BENJAMIN, Montreal, Canada.

A CASE OF RENAL AND URETERAL LITHIASIS IN A CHILD OF THREE YEARS. P. LEREBOULLET, M. BOPPE, J.-E. MARCEL and JEAN BERNARD, Paris méd. **2**:258 (Nov. 4) 1939.

Remarkable recovery of function of the kidney followed operative removal of stones from both kidneys and from the left ureter. There were numerous small stones in the calices of the right kidney, and a large one practically filled the pelvis of the left kidney. The child is being followed carefully with repeated tests for function of the kidneys and with roentgenograms.

LESLIE, Evanston, Ill.

THE PORPHYRINURIAS. A. VANNOTTI, Paris méd. **2**:261 (Nov. 4) 1939.

The author gives an excellent discussion of the metabolism (normal and abnormal) of porphyrin. Of particular interest to the pediatrician is the increase in porphyrin formation in cases of lead poisoning, in which the porphyrin is formed at the expense of the hemoglobin. This may be the case also with other forms of poisoning (arsenic, aniline, phosphorus and mercury) and may occur during treatment with sulfanilamide. LESLIE, Evanston, Ill.

HEMATURIA IN A BOY FIVE YEARS OF AGE. P. NOBÉCOURT, Progrès méd. **67**: 1145 and 1151 (Aug. 19-26) 1939.

The case of a boy of 5 years who had had hematuria since he was 1 year old serves as a background for a discussion of the various causes of hematuria. Nothing new or of special import is contributed, nor was the cause of hematuria in the particular case determined. LESLIE, Evanston, Ill.

BILATERAL HEMORRHAGIC INFARCT OF THE KIDNEY IN AN INFANT. U. CAMILLO, Lattante **11**:33 (Feb.) 1940.

A 9 month old infant after pneumococcic bronchopneumonia and empyema of one month's duration showed marked hematuria and a swelling in the region of the left kidney. Ten days later a similar swelling occurred in the region of the right kidney. Anuria and marked azotemia followed, and death occurred twenty-four hours later. At autopsy marked hemorrhagic infarcts of both kidneys were seen.

HIGGINS, Boston.

URINARY LITHIASIS IN CHILDREN. G. BIANCHI, Riv. di clin. pediat. **38**:129 (March) 1940.

Summaries are given of the cases of 12 children with urinary calculi seen in the surgical clinic at Florence, Italy, between 1910 and 1939. The cases are discussed from the point of view of anatomic pathology, symptomatology, chemistry and therapeutics.

HIGGINS, Boston.

A CASE OF CONGENITAL CROSSED ECTOPIC KIDNEY, NOT FUSED, IN AN INFANT OF FOUR MONTHS. SUZANNE PETRESCO, ONORIU COMAN and EUGENIA AMZA, Med. inf., Bucaresti **1**:355 (Sept.-Oct.) 1939.

At autopsy the two kidneys were found to the right of the vertebral column. The right kidney and adrenal capsule were absolutely normal; the left kidney was in the right ileopelvic region and had a rounded form, with the hilus of the kidney posterior. The two kidneys were separate.

FROM AUTHORS' SUMMARY.

ABORTIVE FORMS OF GLOMERULAR NEPHRITIS. J. GELDRICH, Orvosi hetil. **83**:1056 (Dec. 23) 1939.

Urinalysis was done daily on children with scarlet fever. In 20 patients mild nephritic symptoms arose after the second week of illness. In every case the scarlet fever was mild and the child had no fever before the appearance of the symptoms of nephritis. The alterations were: mild albuminuria, microscopic erythrocyturia and sometimes cylindruria with no signs of renal deficiency. These conditions could be regarded only as abortive forms of acute diffuse glomerular nephritis.

GÖTTCHE, Budapest, Hungary.

Diseases of the Ductless Glands; Endocrinology

OBESITY IN THE RAT FOLLOWING THE INJECTION OF CHROMIC ACID INTO THE HYPOPHYSIS. ALBERT W. HETHERINGTON, Endocrinology **26**:264 (Feb.) 1940.

Experiments are described in which chromic acid was injected into the hypophyses of rats via a parapharyngeal approach. Only 3 of 51 animals so operated on showed any resultant adiposity. All were somewhat dwarfed. Histologic examination revealed extensive damage to the hypothalami and hypophyses of the fat rats.

JACOBSEN, Buffalo.

MACROGENITOSOMIA PRECOX ASSOCIATED WITH HYPERPLASIA OF THE ANDROGENIC TISSUE OF THE ADRENAL AND DEATH FROM CORTICOADRENAL INSUFFICIENCY. L. WILKINS, W. FLEISCHMANN and J. E. HOWARD, Endocrinology **26**:385 (March) 1940.

A case is reported of a 3½ year old boy with precocious development of the genitalia. A sibling was a female hermaphrodite. The patient did not sit alone until the eleventh month. He did not walk until the twenty-sixth month, and then it was noted that he had a stiff, awkward gait. He never learned to talk. From

an early age he was difficult to feed because of a poor appetite. From the age of 1 year he showed marked craving for salt. The parents noticed at birth that the penis and the scrotum were unusually large and that the cry was deep and rough. When he was 5 months old an acneform eruption appeared on his face. At 15 months dark pubic hair began to grow. He was admitted to the hospital for study, where it was found that he was the size of a 6 to 8 year old child and was mentally defective. There were moderate pigmentation of the skin and gums, a low value for blood sodium and a nonprotein nitrogen content varying from 100 mg. to 127 mg. per hundred cubic centimeters.

The authors' summary states: "He died suddenly. The adrenal cortex was composed largely of androgenic or prenatal zone cells, which apparently replaced other elements of the cortex. The testes were large and composed of similar cells. No spermatogenic cells were found. To our knowledge, this is the first case in which there is substantial proof that death from adrenal insufficiency resulted from the destruction of the electrolyte-controlling elements of the adrenals by hyperplasia of the androgenic zone. It supports the theory that the androgenic zone has a function different from the portions of the cortex which control the electrolyte balance. Macrogenitosomia precox has been reported in the male with adrenal tumors. In the case presented it was due to an embryonic hyperplasia of the androgenic zone, and is therefore analogous to the embryonic virilization which causes pseudohermaphroditism in the female." JACOBSEN, Buffalo.

THE EFFECT OF THE THYROTROPIC PRINCIPLE OF THE ANTERIOR PITUITARY ON THE THYROID OF THE UNDERNOURISHED GUINEA PIG. D. J. STEPHENS, Endocrinology **26**:485 (March) 1940.

The author's summary includes the following statements: "Undernutrition in the guinea pig, of sufficient degree to cause a loss of 20 to 30% of body weight in a period of 2 weeks, results in marked structural changes in the thyroid. . . .

"Thyroid of the undernourished guinea pig shows a marked increase in sensitivity to the thyrotropic principle of the anterior hypophysis. In such animals structural changes indicate that the thyroid may be stimulated by the injection of as little as one-tenth the minimal effective dose for normal animals. . . .

"Evidence is presented which suggests that suppression of anterior pituitary function occurs in inanition. It is postulated that the structural changes observed in the thyroid in undernourished animals may be due to decreased secretion of the pituitary thyrotropic principle." JACOBSEN, Buffalo.

THYMUS AND WATER METABOLISM. C. FUMI and E. SARTORI, Riv. di clin. pediat. **38**:65 (Feb.) 1940.

The blood serum of 14 infants with roentgen evidence of thymic hypertrophy showed a normal water content.

After roentgen irradiation, the thymus glands diminished in size; simultaneously there was a 30 per cent diminution in the absorption time in the McClure-Aldrich cutaneous test. An enlarged thymus gland is also a hyperfunctioning gland, as is shown by the water metabolism. HIGGINS, Boston.

TRANSITORY DIABETES IN CHILDHOOD. A. FYKOW, Kinderärztl. Praxis **10**:402 (Sept.) 1939.

The literature on the subject is reviewed. Several authors have described a total of 5 cases in which diabetes was transitory. Fykow reports the observations in 1 of his own patients, a child 2 years of age with pneumonia of the lower lobe of the left lung. After the temperature had returned to normal, the child was still very restless and had symptoms of circulatory failure and Kussmaul breathing. Acetonuria and hyperglycemia were present, even though no sugar was found in the urine for four days. With increasing hyperglycemia, glycosuria also appeared. Treatment with insulin for eight days cured the patient. Dextrose tolerance tests

yielded abnormal blood sugar curves for this patient, for his father and for one of his sisters. A hereditary factor, therefore, was present. Fykow believes that children who show transitory diabetes will probably have permanent diabetes in the future. A diet rather low in content of carbohydrates might prevent this development and should be recommended. HEYMANN, Cleveland.

DIABETES IN CHILDHOOD. OTTOKAR CHIARI, Wien. klin. Wchnschr. **47**:1058 (Nov. 24) 1939.

Chiari (Vienna) points out that all types of hunger diet which might be used in treating diabetes in adults are impossible for children because the growing organism needs more food than mere maintenance intake provided.

In a series of over 200 cases of juvenile diabetes observed by the author it was demonstrated that the disease can be controlled and the patients restored to normal life by administration of insulin and by dietetic treatment. Insulin will always be required, but aside from this and regulation of the diet no special rules of life have to be observed. The most serious difficulty involved is that a tendency toward the disease may be transmitted to offspring, and in spite of the fact that diabetes can be controlled an increase in the diabetic population is not desirable.

As a rule the author recommends hospitalization when a child is found to have diabetes. Usually such patients have marked acetonemia. Through the use of plain insulin and a carbohydrate diet the acetone is eliminated, and the sugar content of the blood and of the urine decreases. Then a balanced diet is built up, while at the same time the excretion of sugar in the urine is strictly controlled at low levels by the administration of insulin. Usually two daily injections of insulin are necessary. When using protamine zinc insulin the author gives one dose in the morning of from 4 to 6 units less than the sum of two injections of regular insulin. Minor variations in the diet are also recommended and suggestions for those variations are presented. Usually this regimen improves metabolism, and it becomes possible to reduce the dose of insulin. ABT, Chicago.

Skin Diseases; Allergy

ERADICATION OF RINGWORM OF THE FEET IN TWO ORPHANAGES: CONTROL AND TREATMENT. H. F. MAGEE and HERBERT A. HARTFIEL, Arch. Pediat. **57**:48 (Jan.) 1940.

The incidence of ringworm in institutions, such as orphanages, can be kept at a minimum if there is thorough and routine inspection of the feet every six weeks to detect evidences of the infection. ORR, Buffalo.

THE UPPER RESPIRATORY REVENGE OF THE ALLERGIC CHILD. I. H. TUMPEER, Illinois M. J. **77**:37 (Jan.) 1940.

The inherent allergic constitution is manifested in infants and children by such conditions as pylorospasm, colic, thymic symptoms, asthma, eczema and hives. These constitutional disorders disturb the progress of growth and development, upset the child emotionally and increase his susceptibility and reactions to infections. Surgical intervention is often resorted to for these combined allergic and infectious disorders, but it serves only to aggravate the condition unless the allergic condition is recognized and relieved. BARBOUR, Peoria, Ill.

STUDIES OF THE ANTIBODIES IN HUMAN HYPERSENSITIVENESS. ROBERT A. COOKE and WILLIAM B. SHERMAN, J. Bact. **39**:62 (Jan.) 1940.

Studies were made by the authors "on the specificity of the skin-sensitizing antibodies found in the natural sensitizations of man, the presence of a 'blocking'

antibody following injections of antigen in such cases and the specificity of this blocking antibody. The method of passive transfer used consists in injecting sensitizing serum into the skin of nonreacting human subjects. After the lapse of 2 days, the sites are tested with antigen. The sensitizing antibody may be neutralized by the addition of sufficient antigen to the serum before injection.

"In cases of human sensitization, multiple reactions as determined by passive transfer are frequent. Using serum from such cases, one antigen often effects neutralization of biologically unrelated antigens. The dominant antigen in the neutralization is usually the one to which the individual is clinically most sensitive. There is evidence of the existence of a blocking antibody which results from the specific injection."

The findings are most interesting, and the authors raise the question "whether the skin-sensitizing antibodies found in human hypersensitiveness are produced solely by antigenic contacts. Certainly, as far as they have been investigated, their specificities do not conform to those of antibody produced in normal animals or man by the injection of antigen."

STOESSER, Minneapolis.

POLLEN ASTHMA AND HAY FEVER IN CHILDREN. SOLKIN C. COPELAND and JOHN P. KEATING, Pennsylvania M. J. **43**:1137 (May) 1940.

This paper makes an attempt, through a clinical survey of 58 pollen-sensitive patients seen in the allergy clinic of the Children's Hospital in Philadelphia during a period of five years, to clarify the problem of recognizing symptoms of pollen sensitivity in youngsters, the method of approaching a diagnosis and the problem of treatment.

LOGUE, Williamsport, Pa.

PHYSIOTHERAPY IN DISEASES OF THE SKIN (PART III). ROBERT AITKEN, Brit. J. Phys. Med. **2**:238 (Sept.-Oct.) 1939.

Among other conditions, the author discusses the treatment of the various forms of nevi. He prefers the use of electrolysis or diathermy to that of solid carbon dioxide in cases of spider nevus. Superficial cavernous nevi respond satisfactorily to treatment with solid carbon dioxide. Treatment with radium is recommended for deep cavernous nevi. These lesions should be treated early in infancy, as they are more radiosensitive at that time.

Pigmented hairy nevi in older children, especially if the hairy element is prominent, should be treated with electrolysis or diathermy. Simple pigmented nevi should be treated with solid carbon dioxide. Good results are reported.

HARTMAN, Cleveland.

A CASE OF ERYTHRODERMIA WITH EPIDERMOLYSIS IN A CHILD TEN YEARS OLD. ROBERT DEBRÉ, MAURICE LAMY and MICHEL LAMOTTE, Bull. Soc. pédiat. de Paris **37**:231 (April) 1939.

A boy 10 years old had diffuse mucocutaneous lesions consisting of large bullae which contained sterile yellowish fluid, areas of erythema and areas of epidermolysis. These were accompanied by fever, and the boy was very sick. He recovered after about ten days, but the cutaneous lesions took somewhat longer to heal and left pigmented areas. The finger nails were shed. There was a high level of excretion of urea, which was considered to be due to extensive tissue proteolysis. The cause of the condition was not definitely determined. In the absence of any evidence of infection a toxic factor was considered likely.

BENJAMIN, Montreal, Canada.

ERYTHEMA NODOSUM IN CHILDHOOD IN TURKEY. I. DOGRAMACI, Ann. pædiat. **154**:357 (March) 1940.

Of 53,000 patients examined during the last five years in the children's clinic of the Model Hospital of Ankara, 90 with erythema nodosum were observed. The maximal incidence was at the ages of 8 to 10 years. A cumulative series of cases was observed in February (13 cases), March (17 cases) and April (10 cases). The number of boys exceeded that of girls by 2. In most of the 39 children tested with tuberculin the reaction was strongly positive, and those reacting negatively did not exceed 4 (10.25 per cent). The author examined 1 patient about two months prior to the eruption, when the reaction to tuberculin was negative. After the eruption it became strongly positive.

The author states that he has no proof that the articular pains represented true rheumatism.

The hypothesis that erythema nodosum is a specific disease is the earliest and still has its advocates. The clinical character of erythema nodosum is comparable with those of other eruptive diseases of infancy. The so-called cases of contagion in the literature constitute another argument in favor of this hypothesis. In 2 of our patients living in the same house and in close contact erythema nodosum appeared with a three day interval. The tuberculin reaction was strongly positive in both cases. One of these patients had given a negative reaction about two months before the eruption, while being treated for malaria, but after the eruption tubercle bacilli were demonstrated in the sputum.

In 1 patient, free from tuberculosis, erythema nodosum followed vaccination against typhoid fever. In this case the author could not attribute the disease to any other factor.

FROM THE AUTHOR'S SUMMARY.

EFFECT OF VITAMIN C IN PYOGENIC INFECTIONS OF THE SKIN IN INFANCY. J. WIRTH, Orvosi hetil. **83**:310 (April 1) 1939.

A Hungarian preparation of vitamin C, "citamino," was given in large doses (50 mg. each), intravenously or intramuscularly, to 20 patients. The author observed a good effect, especially in cases of "primary" pyogenic infections.

GÖTTCHE, Budapest, Hungary.

ANAPHYLAXIS AND AGE. J. AMBRUS and A. RÉTHY, Orvosi hetil. **83**:740 (July 29) 1939.

Young rabbits do not show anaphylactic shock when treated with dead tubercle bacilli, whereas older rabbits always show severe and usually fatal shock. There is therefore some connection between age and anaphylaxis. Anaphylactic shock can also be attained with horse serum, but only in rabbits 41 to 55 days old, whereas younger rabbits show no anaphylactic symptoms even when horse serum is used. The fact that young animals are unable to produce an antigen-antibody reaction can be explained by the underdevelopment of the reticuloendothelial system. It is well known that newborn infants and children do not have certain diseases, but the question is: Are these infants really immune to these diseases, or are they only unable to produce an antigen-antibody reaction? Pirquet, in his famous book "Allergy of Age," was the first to put this question. The authors think that the too early burdening of the organism of young infants with antigen is unnecessary and useless. The immunizations should be postponed until a later age, when the children are able to produce an antigen-antibody reaction, and the vaccinations should be repeated from time to time.

GÖTTCHE, Budapest, Hungary.

Surgery and Orthopedics

COD LIVER OIL DRESSINGS: THEIR MODE OF ACTION. M. LICHTENSTEIN, Lancet **2**:1023 (Nov. 11) 1939.

The local treatment of infected wounds, burns, ulcers, amputation stumps, osteomyelitis, etc., with dressings soaked in cod liver oil or covered with a thick layer of ointment containing in a neutral base (petrolatum) a large amount (25 per cent) of cod liver oil has come into prominence since the publication of Löhr in 1934.

The striking results obtained by many authors with cod liver oil dressings are due, in some degree at least, to the bactericidal power of this substance. Irradiation of cod liver oil enhances this power. Furthermore, the oil is nonirritating to the tissues and supplies them with vitamins.

LANGMANN, New York.

TREATMENT OF BURNS AND SCALDS IN CHILDREN. WALLACE M. DENNISON, Lancet **2**:1107 (Nov. 25) 1939.

The routine treatment is described in detail. A special ward is kept at a constant temperature of 75 F. and fitted with electric cages to supply artificial heat to the patients. After the application of gentian violet to the cleansed area, tannic acid and silver nitrate are used together as coagulants. No dressings or coverings are placed over the coagulum.

In the last five years this treatment has reduced the case mortality rate from about 19 per cent to about 7 per cent and has also resulted in a marked reduction in the incidence of toxemia and sepsis.

LANGMANN, New York.

KYPHOSIS JUVENILIS. O. DITTMAR, Med. Klin. **35**:1203 (Sept. 8) 1939.

The author discusses the pathologic anatomic picture, clinical symptoms and signs, roentgen observations and treatment of the condition and presents six roentgenograms. He observed 88 cases over a period of several years.

SIEMSEN, Chicago.

Miscellaneous

EIGHT YEAR DEPENDENCE ON A RESPIRATOR. SCOTT LORD SMITH, J. A. M. A. **113**:1806 (Nov. 11) 1939.

A 13 year old boy, a victim of poliomyelitis in 1931, has had respiratory assistance by means of a respirator in most of his sleeping hours and many of his waking ones for the past eight years. Beside the psychic depression resulting, his history includes the occurrence of colds, hay fever, eczema, pneumonia, renal calculi and eyestrain.

HEERSMA, Kalamazoo, Mich.

MALIGNANT TUMORS IN CHILDHOOD. HAROLD W. DARGEON, J. Pediat. **15**:317 (Sept.) 1939.

Dargeon presents a brief survey of cancer in childhood. Cancer is a rare disease in childhood, but when compared to many of the common diseases it is found to be a relatively important cause of death, for the mortality rate is extremely high. This paper includes statistics relating to the incidence of malignant tumors in children, the histologic varieties observed, the anatomic frequency of the cancers and the prognosis of the various types of tumors. Methods of diagnosis and treatment are included.

RAUH, Cincinnati.

CANCER OF THE HEAD AND NECK IN CHILDREN. HAYES E. MARTIN, J. Pediat. **15**:363 (Sept.) 1939.

The most frequent cancer of the head and neck in children in Martin's series of 44 cases was retinal glioma. The first symptom of this tumor was dilatation of the pupil, and as the tumor grew it became visible through the dilated pupil as a white reflex, or "cat's eye." The tumor is believed to be congenital, and in over one half of this series of cases the diagnosis was made before the patient reached the age of 2 years. In 75 per cent of the cases the disease was unilateral. Treatment depends on the extent of interference with function of the eye involved. If function of the eye has been completely destroyed, enucleation is the best treatment when only one eye is involved. When both eyes are involved, enucleation should be done on the eye in which greatest loss of function has occurred and irradiation therapy used on the other eye. The next most common location of cancer of the head and neck in children is in the region of the nasopharynx, tonsil and soft palate. The most common first symptom in this series was cervical adenopathy or nasal obstruction, or both. In addition to these tumors Martin discusses nasopharyngeal fibroma, myogenic sarcoma of the soft palate, lymphoepithelioma of the tonsil, cancer of the skin of the face, cancer of the thyroid, osteogenic sarcoma, sarcoma of the tongue and papilloma of the larynx.

RAUH, Cincinnati.

TUMORS OF THE SOFT SOMATIC TISSUES IN INFANCY AND CHILDHOOD. GEORGE T. PACK and THOMAS J. ANGLEM, J. Pediat. **15**:372 (Sept.) 1939.

This paper presents a general description of the various tumors of the soft somatic tissues which may occur in infancy and childhood and the treatment of choice for each type of tumor. Tumors of the peripheral nervous system, the lipomas, liposarcomas, tumors of striated muscle tissue, pigmented nevi, malignant melanomas, glomus tumors, tumors of synovial membrane and tendon sheaths and granulation cell sarcomas are included in the report.

RAUH, Cincinnati.

PROPHYLACTIC EXERCISES FOR CHILDREN. JEROME WEISS and H. J. BEHREND, New York State J. Med. **39**:2044 (Nov. 1) 1939.

Carefully supervised exercises may be given by the mother or by a qualified instructor to preschool children and do much to prevent various postural and other deformities. Some of these exercises require the use of apparatus, while others do not. The exercises should be instituted during the earliest years of life, since it is impossible to determine in which one of a group of apparently normal infants defects will develop later. It is suggested that universal application of systematic and carefully supervised exercises for all infants and children of preschool age would be of great prophylactic value.

Exercises are given especially to strengthen the muscles of the chest, the abdomen and the back. Suitable classes under medical supervision should be established for those able to pay for private instruction and similar facilities made possible in health centers and hospitals for the underprivileged. The exercises described by E. T. Wilkes in his book "Baby's Daily Exercises" (New York, D. Appleton-Century Company, Inc.) are especially advised. This book is said to have gone through but one edition and now to be out of print.

AIKMAN, Rochester, N. Y.

GRAVE ACCIDENTS: PURPURA, ACUTE HEMORRHAGIC NEPHRITIS FOLLOWING THE ADMINISTRATION OF CHENOPODIUM. L. BABONNEIX and A. DEPAILLAT, Bull. Soc. pédiat. de Paris **37**:175 (April) 1939.

An epileptic boy 8½ years old was given three capsules containing 0.25 cc. of oil of chenopodium each, as anthelmintic treatment. The following day he had

severe abdominal pain, melena and purpura. After improvement, recurrence of the condition was observed. He also showed signs of acute hemorrhagic nephritis. There was no vertigo or deafness.

BENJAMIN, Montreal, Canada.

A MEASURING ROD FOR CHILDREN. H. JANET and BARILLON-LAMOTTE, Bull. Soc. pédiat. de Paris **37**:289 (May) 1939.

A measuring rod consisting of a strip of wood fixed to the wall, with a movable rider in the center, was shown. Five graduated columns were marked vertically: a central one to measure height in centimeters, two on the left to indicate the average weight for age for girls and two on the right indicating the average weight for boys.

BENJAMIN, Montreal, Canada.

THE ROLE OF THE GASTROINTESTINAL TRACT IN THE METABOLISM OF QUININE. G. I. LOYBMAN, Vrach. delo **21**:205, 1939.

The purpose of this investigation was to study the role of the gastrointestinal tract in the metabolism of quinine.

One hundred to 150 mg. of quinine hydrochloride was administered to rabbits intravenously. The animals were then killed at various intervals after the administration, and the amount of quinine in the gastrointestinal tract was determined quantitatively by the method of Matolcay.

The author's conclusions were as follows:

1. Quinine administered intravenously appears as early as fifteen minutes afterward in all the divisions of the gastrointestinal tract.

2. From 10.4 to 53.6 per cent of the administered quinine may be found in the intestine.

3. Quinine may be found in the intestine as late as three to four days after its administration by the intravenous route.

4. Only traces of quinine may be found in the stools.

5. Quinine is not destroyed in vitro by the intestinal contents.

6. Absorption of quinine occurs in all the divisions of the gastrointestinal tract.

7. Quinine follows a continuous rotatory course in the organism, namely, from the blood to the gastrointestinal tract and from the latter back into the blood.

8. The diminution of the amount of quinine in the intestine three or four days after administration is due to its gradual destruction in the organism.

BODER, Los Angeles.

Book Reviews

The Structure of the Teeth as Shown by X-Ray Examination. By J. Thewlis. Price, 2s. 6d. net. Pp. 82, with 51 illustrations and 12 tables. London: His Majesty's Stationery Office, 1940.

The author was engaged by the Medical Research Council and the Department of Scientific and Industrial Research to investigate the structure of teeth by means of roentgen rays. The monograph is a well constructed report of this study and is conveniently prefaced by a simple and elementary exposition of the phenomena of roentgen rays, with special reference to diffraction and absorption of the rays. The literature has been reviewed with some care, and a list of well selected references is furnished.

The following excerpts from the general summary give the principal observations.

"X-ray and chemical analysis shows that enamel consists very largely of hydroxy-apatite, $Ca_{10}(PO\,4)\,6\,(OH)_2$. Magnesium and carbon dioxide are also found to be present, and it is suggested that the former replaces some of the hydroxy-apatite calcium and that the latter exists as simple carbonate.

"The hydroxy-apatite is present in the form of submicroscopic crystallites of which the average size is about 0.3μ. Each enamel prism contains, therefore, a multitude of crystallites; and these may, in human enamel, be divided into two groups, so arranged that their axes tend to make angles of approximately 5 degrees and 40 degrees respectively with the prism direction, pointing to that side of the prism remote from the tip of the nearest cusp (the directions being taken away from the tooth).

"The two differently oriented groups of hydroxy-apatite crystallites occur not only in individual prisms but in the interprismatic substance. X-ray and optical examination indicates that the 5 degree group usually predominates in the prism and the 40 degree group in the interprismatic substance. A given portion of enamel rarely contains as many 40 degree as 5 degree crystallites. Indeed the 40 degree group is sometimes entirely absent.

"The phenomena exhibited by enamel prisms when they are examined by polarised light are shown mathematically to be consistent, both in longitudinal and transverse section, with the structure deduced from X-ray measurements. It is also shown that the different colours exhibited by enamel under suitable conditions of examination by polarised light may give an indication of the degree of calcification in this tissue. For accurate work on the degree of calcification, however, a radiographic method is more suitable, and this method has revealed many details of calcification in enamel and dentine."

The areas of enamel which are pigmented or have taken up stain tend to a low degree of calcification. There appears to be a steady increase in the degree of calcification from the dentoenamel junction outward, and in some cases a hypercalcified outer layer was found.

The inorganic material of the dentin is composed of submicroscopic crystallites of hydroxy apatite, the average size of which is about one-tenth that of the crystallites found in the enamel. Examination by the polarizing microscope suggests "spheritic" orientation of the crystals. Occasionally in the translucent root dentin or secondary dentin the crystallites are arranged imperfectly, with their axes approximately parallel to the long axis of the tooth.

A thin layer of the dentin along the dentoenamel junction possesses a relatively low degree of calcification. With this exception, however, the first formed layers are the most highly calcified.

The pulp chamber is found to be almost surrounded by a thin shell of dentin possessing a low degree of calcification. Secondary dentin appears on the whole to be calcified to an extent similar to that of the primary dentin. It appears to be almost entirely separated from the primary dentin by a hypercalcified shell.

"It is possible by a method depending on the quantitative microphotometric comparison of the photographic density of the radiograph of a tooth section with that of the radiograph of an aluminium step wedge obtained under the same conditions, to determine the actual percentage of calcific matter present in enamel and dentine. The degree of calcification may be measured from point to point throughout any desired portion of a tooth, continuous changes may be followed, and 'line' effects may be detected and measured.

"Application of the method to an actual specimen indicates that the percentage of calcific matter present may be estimated to within about 2 per cent, by volume, and variations of this order can also be detected. For a tooth section taken at random it was found, for the areas examined, that the amount of calcific matter present was 91.5 per cent, by volume in the enamel, and 51.5 per cent by volume in the dentine. These figures, however, are not necessarily typical."

The monograph is significant principally in that it furnishes a normal base to which variations produced by particular pathologic changes may be compared by utilizing the same method. Studies of the change in chemical composition and molecular arrangement of the dental calcified tissues may be expected to furnish information of interest from the standpoint of the causation of particular pathologic lesions.

Rheumatic Fever: Studies of the Epidemiology, Manifestations, Diagnosis and Treatment of the Disease During the First Three Decades. By May G. Wilson, M.D. Price, $4.50. Pp. 595, with 125 illustrations. New York: The Commonwealth Fund, 1940.

This volume offers a comprehensive discussion of the problem of rheumatic fever. The author has recorded her own observation, drawn from careful study over a long period of a large number of children suffering from rheumatic fever. Numerous figures and statistical tables supplement the text. Not only does the author present her own observations, but she has recorded the views of many other workers in this field. An extensive bibliography is appended.

The book is divided into five parts, including epidemiology and etiology, clinical and pathologic manifestations, course of rheumatic fever in the first three decades, diagnosis of rheumatic heart disease in children and care and management of the rheumatic child. In the author's discussion of the epidemiology of rheumatic fever, her extensive observations on the importance of heredity in relation to the familial incidence of rheumatic infection are of special interest. In the consideration of the bacterial cause of rheumatic fever, the author attributes less importance to streptococcic infections of the respiratory tract in initiating attacks than a good many other investigators.

Perhaps the most important contribution in the entire book is that which deals with the course of rheumatic fever in the first three decades of life. The author has followed her patients over relatively long periods, many of them from childhood into the third decade of life. The mortality at various stages of the rheumatic infection is recorded. The influence of various factors on prognosis, such as age at onset, nature of the rheumatic manifestations, frequency and severity of recurrences and the importance of changing physical signs, are considered. The status of the surviving patients many years after the onset of the rheumatic infection is discussed. Such a study is extremely valuable as information on the course and duration of rheumatism in juvenile subjects is meager.

This book offers an unusual amount of factual material which should prove of great interest to all students of rheumatic infection.

Child Care and Training. By Marion L. Faegre and John E. Anderson. Fifth edition. Price, $2.50. Pp. 320, with 23 illustrations. Minneapolis: University of Minnesota Press, 1940.

This is a revised edition of the previously issued book. It covers the field of child care, primarily from the point of view of mental and emotional development and training in habits. However, there is an adequate picture of the physical

growth of the normal child. The illustrations are well chosen and attractive. The book is concerned with the child from birth through adolescence, with emphasis on methods or approaches by which good results can be obtained. There is a fine bibliography at the end of each chapter, covering a wide range of pertinent subject material.

The authors, evidently, have drawn their conclusions both from personal experience in the Institute of Child Welfare of the University of Minnesota and from a thoroughgoing study of a well selected group of modern references.

The book can be freely recommended to parents, teachers and child study groups. Physicians who are interested in child care will probably find this an elementary study.

While this work offers little that is new, its contents are well organized and the conclusions forcefully and understandably presented. As a whole, the book is interesting.

Vitamin E: A Symposium Held Under the Auspices of the Nutritional Panel of the Food Group of the Society of Chemical Industry at London, April 1939. Price, $2. Pp. 88, with 2 illustrations and 12 tables. New York: Chemical Publishing Company, 1940.

This monograph represents the proceedings of the symposium on vitamin E, edited by A. L. Bacharach and J. C. Drummond. It is a concise and authoritative summary of existing knowledge concerning this important and intriguing vitamin, intriguing because this so-called antisterility vitamin has not been shown to be related to the "sex hormones," either chemically or physiologically.

The monograph is divided into three parts: part I, the chemical structure and properties of tocopherol (vitamin E), including chemical methods of assay; part II, the physiologic action of the vitamin and the consequences of vitamin E deficiency, with observations on the biologic estimation of the vitamin, and part III, the clinical and veterinary uses of vitamin E preparations.

The pediatrician who reads this monograph will almost surely benefit from the impressive amount of information concerning this vitamin that the chemists and physiologists have acquired. He will also be struck by the contrast between the precise knowledge presented by these contributors and the contradictory and unsubstantiated opinions expressed in those sections that deal with human therapy.

Endocrine Therapy in General Practice. By E. L. Sevringhaus. Third edition. Price, $2.75. Pp. 238, with 49 illustrations. Chicago: The Year Book Publishers, Inc., 1940.

This book, primarily written for the general practitioner, was so well received that a new edition has become necessary. The new book, thoroughly revised, retains the chief merits of the previous edition. It acquaints the physician with the practical applications of endocrinology. The author undertakes this difficult task with a well balanced attitude, keeping in mind the role of the hereditary background of the patient, his environment and particularly his nutrition.

An introductory chapter on systematic endocrinology reviews briefly the function and role of each endocrine gland and its hormones. The pediatrician will be chiefly interested in a new chapter on endocrine problems in childhood and adolescence. The problems of growth, of precocious and delayed puberty and of obesity are briefly discussed. The chapter on dietary treatment of obesity deserves special attention, since the scientific basis as well as the technical side of reducing diets are well presented. Consideration is also given to the physiologic, psychic and economic difficulties encountered by the patient on such a diet.

L'irradiazione del timo. By Maria Pellini. Price, none given. Pp. 91, with 27 illustrations. Bari, Italy: Tipografia Alfredo Cressati, 1939.

A short, clearcut discussion of the anatomy, physiology and radiobiology of the thymus is followed by a consideration of the therapeutic irradiation of that gland.

The three types of thymic hyperplasia are: (1) that involving the thymus alone, (2) that associated with status lymphaticus and (3) that associated with exophthalmic goiter. The first type is the most common in children.

Thymic death is probably due to pressure on nerves rather than to asphyxiation or autointoxication from lymphatic dyscrasia.

In seven years of radiologic experience in a large pediatric clinic (Milan), only 4 cases came to the author's personal attention, indicating that thymic hypertrophy with symptoms is certainly rare.

Benefit is sometimes obtained from irradiating an abnormally functioning thymus, as in patients with myasthenia and psoriasis.

Irradiation of the thymus when dysfunction of other endocrine glands is also present is beneficial in adolescent boys with obesity and retarded genital development and occasionally of benefit in patients with exophthalmic goiter and scleroderma.

Estudios sobre la etiologia enfecciosa de las diarrheas infantiles. By several authors, under the editorial direction of J. Garcia Morales. Price, none given. Pp. 163, with 29 tables. Montevideo, Uruguay: Society of Pediatrics, 1940.

This 140 page monograph begins with a consideration of the importance of infection as a cause of summer diarrhea. Of the 1,816 cases studied, 1,611 were selected for statistical purposes. Clinically, three types of summer diarrhea are recognized, namely, choleriform, dysenteric and mixed. In more than half the cases, the etiologic agent was determined as either Salmonella or Shiga's bacillus. In adults and children over 3 years of age the mortality is practically nil, but in those under 1 year, enteritis from Shigella has a mortality of 45 per cent and that from Salmonella a mortality of 30.7 per cent.

In a separate study of parenteral infection from these groups of organisms, meningitis, osteomyelitis and arthritis were found to be the most frequent. An extensive review of the literature is given. The several studies making up this monograph are summarized and translated into French, English and German.

Simplified Diabetic Manual. By Abraham Rudy, M.D. Price, $2. Pp. 216, with 9 illustrations. New York: M. Barrows & Company, 1940.

The distinctive feature of this diabetic manual is that it includes, in addition to treatment of the usual subjects, some excellent international recipes.

The short chapter on juvenile diabetes recognizes the increased need for protein and carbohydrate in the child's diet and mentions the difficulties arising in adolescence. A sample diet and school luncheon are shown.

Also of pediatric interest are the chapters on "Marriage in Diabetes" and "Diabetes in Pregnancy." The future mate should always be informed of the presence of diabetes. A brief discussion of the problems of the newborn infants of diabetic mothers is especially interesting because of the controversy over the abnormalities and treatment of these babies.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
General Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Assistant Secretary-Treasurer: Dr. Charles F. McKhann, University of Michigan, Ann Arbor, Mich.

Canadian Committee:

Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston, Mass. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

British Paediatric Association

President: Prof. Charles McNeil, 44 Heriot Row, Edinburgh, Scotland.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandsche Vereeniging voor Kindergeneeskunde

President: Prof. Dr. J. van Lookeren Campagne, Hofstraat 16, Gröningen, Holland.
Secretary: Dr. R. P. van de Kasteele, Laan van Poot 340, 's Gravenhage, Holland.
Place: Different places. Time: Three times a year.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

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*Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRÍA

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Jorge Muñoz Turnbull, Av. Alvaro Obregón 186, Mexico, D. F.
Secretary: Dr. Fernando López Clares, Medellín 191, Mexico, D. F.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Conrado Pelfort, Av. 18 de Julio 1246, Montevideo.
Secretary: Dr. Héctor Mourigan, Av. 18 de Julio 2175, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Julius H. Hess, 104 S. Michigan Ave., Chicago.
Secretary: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Place: Cleveland. Time: June 2-6, 1941.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. J. B. Bilderback, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Statler Hotel, Boston. Time: Oct. 9-11, 1941.
Region I. Place: New Haven, Conn. Time: March 27-29, 1941.
Region II. Place: Richmond, Va.
Region III. Place: Palmer House, Chicago. Time: May 15-17, 1941.
Region IV. Place: Fairmont Hotel, San Francisco. Time: May 1-3, 1941.

NORTHERN CALIFORNIA AFFILIATES

President: Dr. Crawford Bost, 490 Post St., San Francisco.
Secretary: Dr. William A. Reilly, 384 Post St., San Francisco.
Time: Second Thursday of September, November, January, March and May.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

Chairman: Dr. D. L. Richardson, 593 Eddy St., Providence, R. I.
Secretary: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.

American Pediatric Society

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Place: Hot Springs, Va. Time: May 22-24, 1941.

Canadian Society for the Study of Diseases of Children

President: Dr. L. M. Lindsay, 815 Medical Arts Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. A. Ashley Weech, 3975 Broadway, New York.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. R. Cannon Eley, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. S. G. Henricke, 4215 N. E. Hancock St., Portland, Ore.
Secretary: Dr. J. S. Backstrand, 333 Wyatt Court, Salem, Ore.

Rocky Mountain Pediatric Society

President: Dr. Donn Barber, 802½–8th Ave., Greeley, Colo.
Secretary: Dr. Kenneth Schmidt, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Harvey F. Garrison, 319 E. Capitol St., Jackson, Miss.
Secretary: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables, Fla.

STATE

Alabama Pediatric Society

President: Dr. M. V. Adams, 803 Government St., Mobile.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. William Belford, 233 A St., San Diego.
Secretary: Dr. John J. Miller Jr., 2398 Sacramento St., San Francisco.
Place: Del Monte. Time: May 1941.

Florida State Pediatric Society

President: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables.
Secretary: Dr. George N. Leonard, 605 Lincoln Rd., Miami Beach.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. R. C. McGahee, 1345 Greene St., Augusta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. D. C. Darrow, 789 Howard Ave., New Haven.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Orville Barbour, 331 Fulton St., Peoria.
Secretary: Dr. Craig Butler, 715 Lake St., Oak Park.
Place: Chicago. Time: May 1941.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Blvd., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

Louisiana State Pediatric Society

President: Dr. H. Aubrey White, Alexandria.
Secretary-Treasurer: Dr. W. C. Rivenbark, 3503 Prytania St., New Orleans
Place: Shreveport. Time: April 1941.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Norman L. Hawkins, 11 Public Sq., Watertown, N. Y.
Secretary: Dr. William J. Orr, 135 Linwood Ave., Buffalo.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.
Secretary: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Place: Pittsburgh. Time: Sept. 29-Oct. 2, 1941.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Harry Towsley, University of Michigan Hospital, Ann Arbor.
Secretary: Dr. Leon DeVel, 110 E. Fulton, Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.
Place: Biloxi. Time: May 12, 1941.

Nebraska Pediatric Society

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

New Hampshire Pediatric Society

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

North Carolina Pediatric Society

President: Dr. Marion Y. Keith, 369 N. Elm St., Greensboro.
Secretary: Dr. G. W. Kutscher Jr., 176 Woodfin St., Asheville.

Oklahoma State Pediatric Society

President: Dr. Ben H. Nicholson, 301 N.W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

South Carolina Pediatric Society

President: Dr. R. B. Josey, 1517 Hampton Ave., Columbia.
Secretary-Treasurer: Dr. Wilson Ball, South Carolina State Health Dept., Columbia.

Tennessee State Pediatric Society

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Secretary: Dr. Gilbert Eblen, 611 W. Main Ave., Knoxville.

Texas Pediatric Society

President: Dr. C. P. Jasperson, 509 Nixon Bldg., Corpus Christi.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Fort Worth. Time: May 14, 1941.

Virginia Pediatric Society

President: Dr. John M. Bishop, 511 Medical Arts Bldg., Roanoke.
Secretary: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Raymond Sloan, 1139–4th Ave., Huntington.
Secretary: Dr. Thomas G. Folsom, 1139–4th Ave., Huntington.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

Bronx Pediatric Society

President: Dr. Harry S. Altman, 940 Grand Concourse, New York.
Secretary: Dr. David Zahn, 2474 Valentine Ave., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Archibald Smith, Garden City, N. Y.
Secretary: Dr. Walter Coles, 604–2d St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Tuesday of April and September.

Chicago Pediatric Society

President: Dr. Philip Rosenblum, 2376 E. 71st St., Chicago.
Secretary: Dr. Bengt Hamilton, 826 E. 61st St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. Edgar Loomis, 351 W. Jefferson Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. Robert J. Mason, 460 Birmingham Rd., Birmingham, Mich.
Secretary: Dr. J. Hugh Lewis, 2966 Biddle Ave., Wyandotte, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Stephen C. Redd, 157 Forrest Ave. N. E., Atlanta.
Secretary: Dr. C. Dixon Fowler, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Thomas J. Donovan, 3820 Fannin St., Houston, Texas.
Secretary: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. John Aull, 1103 Grand Ave., Kansas City.
Secretary: Dr. George Herrman, 1107 Bryant Bldg., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Alonzo Cass, 1908 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Gladys Patric Shahovitch, 3936 Roderick Rd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Sydney Nussbaum, 247 Ocean View Ave., Brooklyn.
Secretary: Dr. Harry Bikoff, 850 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., second Monday of each month, October to March, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. A. A. Trivilino, 88-07–150th St., Jamaica, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry A. Ong, 1801 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. William F. Burdick, 5402 Connecticut Ave. N. W., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

Memphis Pediatric Society

President: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. R. P. Schowalter, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. George H. Wegmann, 2650 W. Hopkins St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Leslie O. Ashton, 850 Park Ave., New York.
Secretary: Dr. Alfred Langmann, 108 E. 68th St., New York.
Place: New York Academy of Medicine, 2 E. 103 St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Harold Flanagan, 711 Lowry Medical Arts Bldg., St. Paul, Minn.
Secretary-Treasurer: Dr. Everett C. Perlman, 620 Medical Arts Bldg., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. J. Byron Snow, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: Third Friday of each alternate month.

Philadelphia Pediatric Society

President: Dr. Pascal F. Lucchesi, 4000 N. Front St., Philadelphia.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. E. L. Piper, 3200–5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. Carl Ruder, 646 Washington Rd., Mount Lebanon, Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Charles L. Outland, 312 N. 9th St., Richmond, Va.
Secretary-Treasurer: Dr. T. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. W. L. Bradford, 16 N. Goodman St., Rochester, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: First Friday of each month from October to June.

Seattle Pediatric Society

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Secretary: Dr. Donald C. Shelby, 3780 Wilshire Blvd., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Mark Osterlin, Central Michigan Children's Clinic, Traverse City, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Time: Nov. 15-16, 1940.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. M. Bernard Brahdy, 531 E. Lincoln Ave., Mount Vernon.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Ave., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.

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